MBL - Newsletter

The Insight dive of MBL's cutting-edge Diagnostics

MICROBES SINCE 1977

Volume 1 Issue : 1 October 2023

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12 Pages

Unveiling the Cutting-Edge World of Clinical Diagnostics

Upcoming Event

CME

Date : **October 8th, 2023**

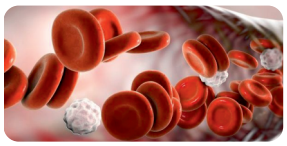
Time : **6.30pm - 8.30pm**

Venue: **Hotel Burma Kadai, Virudhunagar**

Dear Readers,

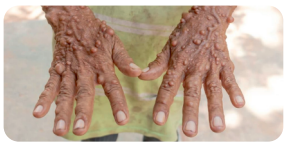
Connecting with all of you is a pleasure indeed. We are thrilled to welcome you to the premiere issue of our newsletter, where we embark on an enlightening journey through the world of medical case reports. In this inaugural edition, we dive deep into five unique cases that span the spectrum of medical complexities.

Inside this Issue



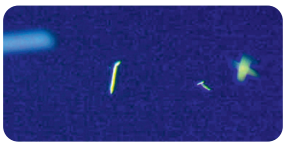
Von Willebrand Disease

Explore a case that unravels the challenges in diagnosing and managing this inherited bleeding disorder. We delve into the intricacies of blood clotting and the pursuit of tailored treatment strategies.



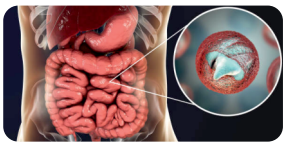
Neurofibromatosis 1 - Microdeletion Syndrome

Witness the story of a rare genetic syndrome, illuminating the importance of genetic testing, early detection, and holistic care for patients with complex conditions.



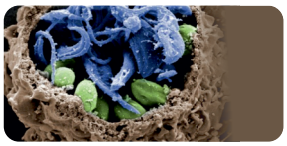
Gouty Arthritis

Follow a patient's journey through the excruciating pain of gouty arthritis. Discover the science behind gout, its triggers, and effective pain management strategies.



Gonococcal Bacteremia

Uncover the diagnosis and treatment of a case that underscores the evolving challenges of antibiotic resistance and the critical importance of safe sexual practices.



Cryptosporidium spp in a Young Healthy Female

In a surprising twist, explore a case of Cryptosporidium infection in an otherwise healthy individual, shedding light on the need for vigilance in water safety and hygiene practices.

Through these case reports, we aim not only to inform but also to inspire. Each case represents a unique puzzle that dedicated healthcare professionals have untangled, showcasing the power of medical knowledge, teamwork, and innovation. As we navigate the intricacies of these medical narratives, we encourage you to engage with us. Share your thoughts, questions, and experiences. Your feedback will be the compass guiding our future issues, ensuring that we continue to deliver content that informs, educates, and empowers.

Thank you for joining us on this remarkable journey into the heart of medicine. We look forward to sharing more enlightening cases, expanding our understanding, and fostering a sense of community in the world of healthcare.

Warm regards,

Dr. M.Jayahar Bharathi, Ph.D.,
Dr. Deepasankari.T.L., MBBS., MD.,

MD's Message

Founder - Microbiological Laboratory

Greetings,

Dear Friends, I am delighted to address you in this issue of Microbiological Laboratory's Newsletter. As the President of our esteemed institution, it is both an honour and a privilege to share with you our ongoing commitment to excellence in the fields of Molecular Diagnostics, Genetic & Coagulation testing, Microbiology & Serology, and Histopathology.

Our Multidisciplinary Approach:
A Source of Strength:

At MBL, we take pride in our ability to seamlessly integrate multiple clinical disciplines to provide comprehensive diagnostic insights. This multi-disciplinary approach is a testament to our dedication to delivering the highest quality patient care.

Molecular Diagnostics:
Pioneering Personalized Medicine:

Our Molecular Diagnostics division continues to lead the way in the era of personalized medicine. Through genetic analysis and innovative diagnostic techniques, we are revolutionizing patient care by tailoring treatments to individual genetic profiles.

Coagulation Studies:
Navigating the Complexities of Hemostasis:

The intricacies of Coagulation Studies are at the heart of patient care in many clinical scenarios. We remain committed to advancing our knowledge and technology in this field to better serve our patients and healthcare partners.

Microbiology:
Combating Infectious Challenges

In the face of emerging pathogens and antibiotic resistance, our Microbiology division remains steadfast in its pursuit of accurate and timely diagnostic solutions. We are dedicated to supporting infection control, guiding antibiotic therapy, and improving patient outcomes.

Histopathology:
Revealing the Microscopic Story

Histopathology is the cornerstone of our understanding of disease at the cellular level. Our talented pathologists work diligently to uncover the intricate details within tissues, aiding in precise diagnoses and treatment planning.

A Special Note of Thanks

I would like to express my deepest gratitude to our dedicated staff, whose unwavering commitment to excellence drives our success. It is their expertise, passion, and tireless efforts that enable us to push the boundaries of clinical diagnostics.
In closing, I extend my sincere appreciation to our readers, patients, and clinicians, for continued support. Together, we are making a difference in healthcare.

> "Together, we are making a difference in healthcare

Mariappa Mani,
Managing Director,
Microbiological Laboratory

Case Report 1
Cryptosporidium spp in a Young Healthy Female

Authors : Dr Deepasankari T L, Dr. Shakeerabanu

A 18 yr old female presented to Gastro OPD with complaint of acute diarrhoea for 3 days, No H/o vomiting or fever or abdominal pain, past H/o recurrent urinary tract infection which was treated. This young girl resides at a hostel, in well reputed institution at Coimbatore. No H/o diabetes, chronic renal failure, hypertension, thyroid issues, genetic disorder or immunocompromised status or autoimmune disease. She was initially treated with combination of two antibiotics but there was no clinical improvement and the diarrhoea persisted.

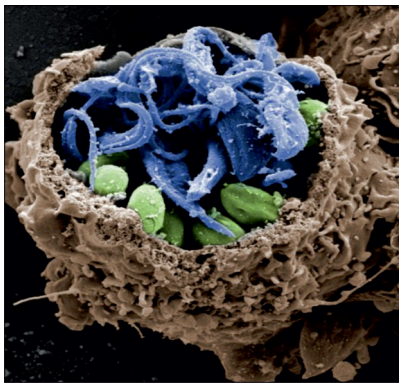
In, bacterial stool culture no significant pathogens were isolated and the stool sample was sent for combined gastroenteritis multiplex PCR to look for any non – cultivable bacteria, viral or parasitic etiology at Microbiological Laboratory, Coimbatore, Veerakeralam processing location. **In Multiplex PCR - Cryptosporidium spp DNA was detected**. Patient was treated with Nitazoxanide 500 mg BID x 3 days, she was clinically better after the first dose of Nitazoxanide.

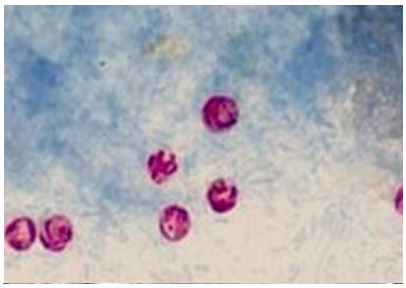
Discussion:

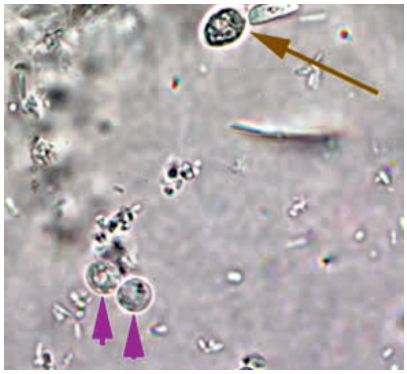
Cryptosporidium is a leading cause of waterborne diarrhoeal disease among the humans in the world, it is a microscopic parasite causing cryptosporidiosis. Both the parasite and the disease are commonly known as "Crypto." Many species of Cryptosporidium can infect animals, some of them can infect humans. The parasite has a protective outer shell that allows to survive outside the body for longer periods of time and makes it very tolerant to chlorine disinfection.

Mode of transmission:

Parasite can be spread in different ways like water (drinking water and recreational water) is the most common way to spread the parasite. Symptoms of cryptosporidiosis generally begin 2 to 10 days (average 7 days) after becoming infected with the parasite. The most common symptom of cryptosporidiosis is watery diarrhoea, stomach cramps or pain, dehydration, nausea, vomiting, fever, weight loss.







Know the Facts

Practice Good Hygiene everywhere by washing the hands with soap and water (Alcohol-based hand sanitizers are not effective against Crypto)

Clean, sanitize/ disinfect toys and surfaces to prevent germs from spreading easily.

Notify the administrators if the canteen staff / food suppliers/ health care workers are suffering from diarrhoeal disease.

At the pool, lake, and other places "Do not swim or let kids swim if diarrhoea is present". (If crypto is diagnosed, restrict - 2 weeks to go swimming after diarrhoea has stopped).

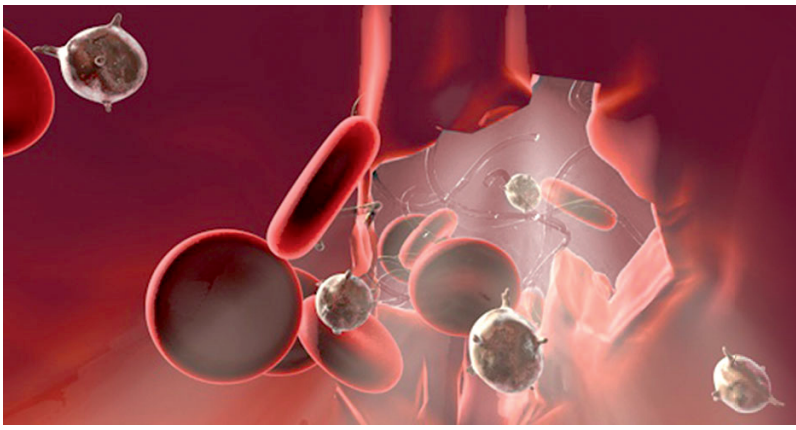
Practice Extra Caution While Travelling

References :
1.https://www.cdc.gov/parasites/cryto/illness.html
2.https://my.clevelandclinic.org/health/diseases/21023-cryptosporidiosis

Case Report 2

A rare case of Type 3 Von willebrands disease work up in an Antenatal woman

Authors : Dr Dominic, Dr Vani Jayaraj, Dr Nagabhushan Vellala, Mrs Bhakiyam, Mrs Veera Pappammal



Test Performed : 1. VWF
2. APTT
2. APTT Mixing studies
3. RICOF
5. RIPA
4. Factor VIII

Principle : Clot-based Assay/ ELFA

TAT : 4hrs

Background

Von Willebrand disease (vWD) is the most common inherited bleeding disorder worldwide. Genetic mutations in the von Willebrand gene may result in either quantitative (Types 1 and 3 vWD) or qualitative defects (Type 2 vWD) of von Willebrand Factor (vWF) an adhesive and multimeric glycoprotein, which is essential for the normal haemostasis Type 3 is the rarest and most severe form of vWD, resulting in a virtual absence of vWF. Clinical manifestations are mainly represented by muco-cutaneous and soft tissue bleeding and the severity of bleeding symptoms is variable depending on the degree of VWF and FVIII reduction, as well as other factors

Case Details

Age : 24 year/ Female,

Primi Gravida(36 weeks GA)was admitted in tertiary care hospital for delivery. She presented with prolonged APTT. She had been symptomatic from 1 year of age with easy bruisability,echymotic patches,gum bleeding .She had menorrhagia after puberty and was diagnosed to have bleeding VWF disease in CMC vellore though work up details were not available. She apparently received transfusions blood and cryoprecipitate from local hospitals during bleeding episodes since childhood.

Family History:

Born out of second degree consanguious marriage. No history of bleeding diathesis

Interpretation:

The patient had normal blood counts with prolonged APTT and bleeding time.The APTT mixing studies revealed immediate correction with normal pooled plasma indicating coagulation factor deficiency. Prolonged bleeding time indicated a defect in primary hemostasis. As expected VWF antigen levels were undetectable, along severely low RICOF and Factor VIII levels confirming the diagnosis VWF Type 3 disease.

Discussion:

In healthy women and in type ,VWF antigen anf factor 8 levels increases during pregnancy .Women with type 3 VWD typically do not show any increase of FVIII and VWF during pregnancy because their endothelial VWF stores are lacking. Thus VWF/FVIII concentrates may be required during pregnancy to control bleeding during delivery or for Cesarean section and also post partum

Conclusion :

Pregnancy in Von Willebrand's disease may carry a significant risk of bleeding. Hence work up of a women presenting with symptoms of bleeding diathesis and deranged coagulation test should be worked up systematically to prevent catastrophies during antenatal as well as time of delivery.

References :

1.Jill M Johnsen, Sarah Ruuska, Peter A. Kouides, Barbara A. Konkle,Design of the Von Willebrand Factor in Pregnancy (VIP) Study,Blood,Volume 136, Supplement 1,2020,Page 29

2. Mamatha Mandava, John Lazarchick, Emily Curl, Shayla Bergmann; A Unique Case of Type 3 Von Willebrand Disease. Blood 2018; 132 (Supplement 1): 5031. doi

Coagulation Profile

Bleeding

Detection and Management of bleeding disorders

Specimen Info

- **Specimen Type** : Citrate plasma
- **Volume** : Citrate tubes filled up to the specified mark
- **Special Instruction** : Separate plasma & freeze immediately at -20° C for all coagulation tests (except Platelet Aggregometry)

Panel info

- **Prothrombin Time** (PT)
- **Activated Partial Thromboplastin time** (APTT)
- **Thrombin Time** (TT)
- **Mixing studies :** PT & APTT
- **Fibrinogen**
- **Factor VIII**
- **Factor IX**
- **Factor XI**
- **Von Willebrand factor Antigen** (VWF)
- **Ristocetin Cofactor Assay** (RICOF)
- **Ristocetin Induced Platelet Aggregation** (RIPA)
- **Prolonged APTT work up for Bleeding patient**
  - APTT Mixing studies
  - Factor VIII
  - Factor IX
  - Factor XI
  - Von Willebrand Factor antigen (VWF)
  - Ristocetin Cofactor
  - Ristocetin Induced Platelet Aggregation
- **Hemophilia Panel**
  - Factor VIII
  - Factor IX
  - Factor XI
  - APTT mixing studies
- **Platelet Aggregometry**
  - Collagen
  - Adenosine Diphosphate
  - Arachidonic Acid
  - Ristocetin
- **Von Willebrand factor Panel**
  - Von Willebrand factor
  - Factor VIII
  - Ristocetin Cofactor Assay (RICOF)
- **Platelet functional disorder \VWD Work up**
  - Prothrombin Time (PT)
  - Partial Prothrombin Time (PPT)
  - Thrombin Time (TT)
  - Fibrinogen
  - INR
  - Factor VIII
  - Von Willebrand Factor
  - Von Willebrand Factor antigen (VWF)
  - Platelet Aggregation :
    - Adenosine Diphosphate
    - Ristocetin Cofactor
    - Arachidonic acid
    - Collagen

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The Art of Diagnostics
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Version 1.0 | 21.09.2023

Case Report 3

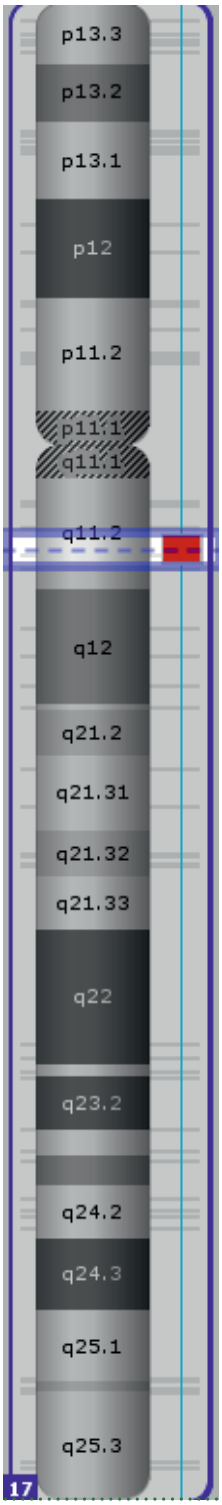
Neurofibromatosis1-Microdeletion syndrome detected by Chromosomal micro array

Authors - Dr Vani Jayaraj, Dr Shakeera Banu, Dr Senthil Raja, Mrs Shyni Rajasekar, Mrs Srividya G

Age/sex : 6Y & Male
Specimen : Whole Blood
Clinical Details : Global developmental delay, umbilical hernia, small angle alternating esotropia, Preauricular tag, multiple cafe-au-lait spots ,To rule out Neurofibromatosis.
Results Abnormal microarray Result (Male). 17q11.2 deletion (Neurofibromatosis 1 Microdeletion syndrome)

Interpretation :
The whole genome SNP Microarray copy number analysis showed an abnormal result. The analysis showed an **interstitial deletion (1 copy present)involving chromosome 17 within 17q11.2.** This region contains around 24 genes including the NF1 gene which is responsible for NF1 microdeletion syndrome. Thus the result is consistent with a clinical diagnosis of **17q11.2 syndrome**.

Discussion :
A Neurofibromatosis 1 (NF1, OMIM 162200) is an autosomal disorder with an estimated incidence of 1 in 3500 live births NF1 is due to autosomal dominant loss-of-function mutations of the NF1 gene (neurofibromin 1)located at 17q11.
Approximately 5 to 20% of all patients with Neurofibromatosis Type 1 carry a heterozygous deletion of approximately 1.4 Mb involving the NF1 gene and contiguous genes lying in its flanking regions. NF1 microdeletion syndrome is often characterised by a more severe phenotype than that observed in the majority of NF1 patients. In particular, patients with NF1 microdeletion show variable facial dysmorphism, mental retardation, developmental delay, Café au-lait spots and excessive number of early onset neurofibromas



Images of the patients SNP array profile showing copy number variation in 17q11.2 region which contains around 24 genes including the NF1 gene(black arrows)

> “ Patients with Nf1 have a **50%** risk for having a child affected with NF1

Conclusion :
In conclusion,CMA is a valid methodology for clinical testing.It is equivalent to performing hundreds of subtelomeric and locus specific FISH probes and offers efficient and high through put alternative for detecting genomic imbalances associated with a wide range of developmental disabilities including congenital malformations, cognitive impairment, and behavioral abnormalities CMA has replaced Giemsa-banded karyotype the first-tier test for genetic evaluation of children with developmental and behavioral disabilities.

References :
1.Beaudet AL. The utility of chromosomal microarray analysis in developmental and behavioral pediatrics. Child Dev. 2013 Jan-Feb;84(1):121-32. doi: 10.1111/cdev.12050. Epub 2013 Jan 11. PMID: 23311723; PMCID: PMC3725967.
2.Kehrer-Sawatzki, H., Cooper, D.N. Classification of NF1 microdeletions and its importance for establishing genotype/phenotype correlations in patients with NF1 microdeletions. Hum Genet 140, 1635–1649 (2021). https://doi.org/10.1007/s00439-021-02363-3

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World class Result Interpretation

Microbiological Laboratory

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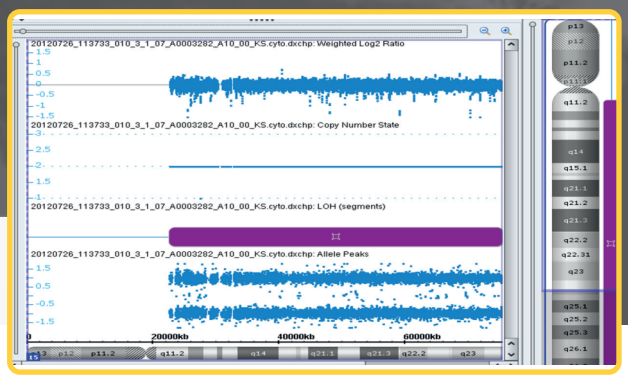
Karyotype and FISH are not enough!

Chromosomal Microarray

(Optima Suite)



Chromosomal Microarray is the first FDA-cleared whole-genome diagnostic test to aid physicians in identifying the underlying genetic cause of developmental delay, intellectual disability, congenital anomalies, or dysmorphic features in children.

Why MBL CMA?

Analyze the **whole human genome** with **high resolution**

Streamlined **data analysis**

Accurate identification of a number of **chromosome disorders early** in **pregnancy**

Ability to **detect** high resolution **DNA CNV, GAINS, LOSSES UPD & LOH**

Specimen Info

1. Extracted **DNA** samples (1µg - 2µg)
2. **POC** (Product of conception) 100-200g
3. **EDTA Blood** (2-3ml)
4. **CVS** Sample/ **Amniotic Fluid**/ Cultured Cells

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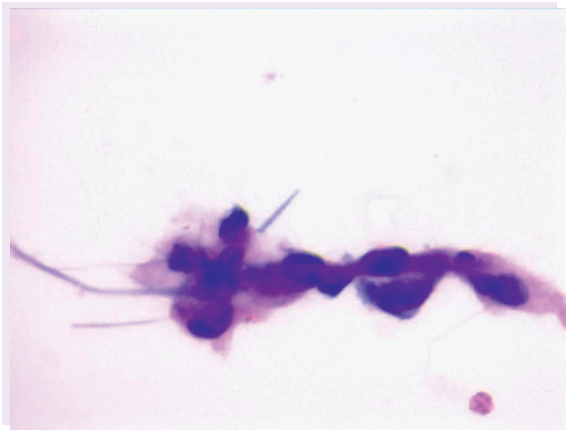
Version 1.1 | 08.06.2023

Case Report 4

A rare case of urate deposits in Breast cyst fluid

Authors : Dr Krishna V, Dr Nagabhushan



Introduction:

Gouty arthritis can occur in and around many joints in the body; recently monosodium urate (MSU) crystals have been demonstrated in many other soft tissues.

Objective:

To present a rare case of MSU crystals in breast.

Materials & Methods:

A 46 year old female presented with cystic lump breast. About 4 ml of off white, turbid and nonviscous fluid was aspirated.

Wet mount examination of the fluid revealed needle shaped birefringent monosodium urate crystals by polarization microscopy. The background was consistent with benign cytologic picture. Retrospectively we were informed that uric acid level measured in the cyst fluid is 42.5 mg/dl

Results:

Mostly MSU crystals are long with parallel sides and blunt ends. exhibiting parallel sides with one blunt end and others less blunt but not truly needle-like. Apparent stacking of crystal components is also seen.

In our case , the crystals were compatible with the above described morphologic characteristics.

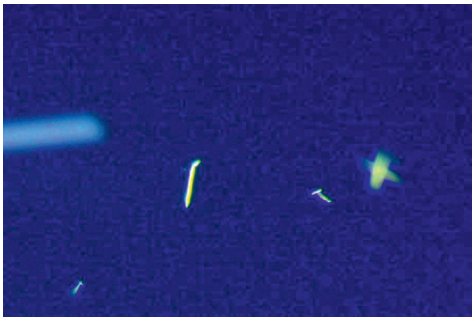
Discussion:

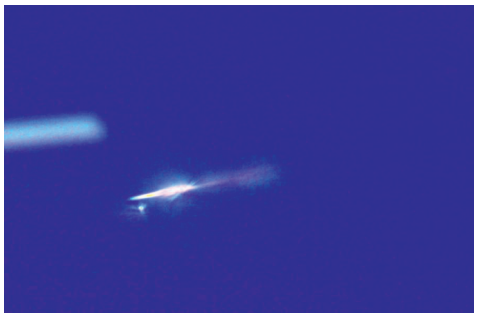
Review of literature reveals that 5 cases of crystals in breast cyst fluid has been documented in the literature.

Diagnostic dual energy computed tomography (DECT) has now revealed that urate deposits is not uncommon in extra -articular tissues such as finger pulp, bronchi, nose, larynx, eye, nail, breast & even in the intestine & heart, including cardiac valves, vasculature and one case in scrotum.

Conclusion:

To our knowledge, this case is one of the very few reported cases of MSU crystals in the breast and is a case of occult systemic gout. The awareness of the possibility of breast involvement in gout is important as treatment modality exceeds the capacity of rheumatologists and is taken over by multidisciplinary team.





References:

1. Tophi, Thomas Bardin MD, in Gout, 201

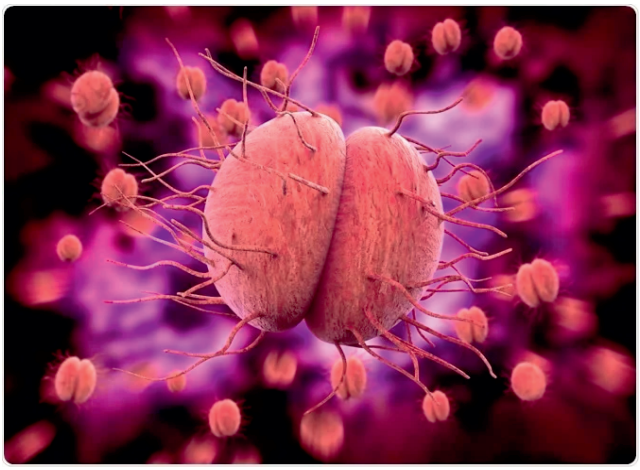
2. Flores Martín JF, Vázquez Alonso F, Puche Sanz I, Berrio Campos R, Campaña Gutierrez MA, Cózar Olmo JM. Gouty tophi in the penis: a case report and review of the literature. Case Rep Urol. 2012;2012:594905. doi: 10.1155/2012/594905 [PMC free article] [PubMed]

Case Report 5
Gonococcal bacteremia in a pediatric patient

Authors : Dr Madhuri Rathi Maheshwari, Dr Senthil Raja

Age/ Sex : 12yrs/ Female

Test requested : Endocarditis PCR panel, multiplex real time PCR



A blood sample was received for infective Endocarditis PCR panel, multiplex real time PCR, from a 12-year old female child, with a history of on and off fever since a month, and not responding to any medications. She was a known case of Tetralogy of fallot (TOF) and TOF repair was done in 2015. Repeated blood cultures done at local hospital and were negative.

Infective endocarditis PCR panel was performed - **Neisseria gonorrhoeae DNA was detected**. For reconfirmation, we have requested the clinician to send second blood sample on very next day, which was also turned out to be positive for Neisseria gonorrhoeae.

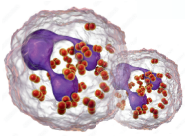
Discussion:

Gonorrhea is all diseases caused by Neisseria gonorrhoeae. **Pre-pubertal child** is more **susceptible to N. gonorrhoeae infection** because the vagina is alkaline and contains no estrogen. Gonorrhea vaginitis is the most common form of gonorrhoea in prepubertal children beyond neonatal period. Transmission in child can be through sexual contact (abuse) or non-sexual contact. Gonorrhea vaginitis in children more often asymptomatic, with clinical manifestation such as mucopurulent discharge, vaginal pruritus and vulval erythema. Supporting examination comprise of gram staining from vaginal discharge, culture and nucleic acid amplification testing. 1 In this patient, a port of entry of infection could not be identified as we did not receive urogenital or any other sample, further.

Depressing Facts

Gonococcal bacteremia is a rare condition affecting **<3% of patients** with gonorrhoeae.

It is possible that **prolonged asymptomatic carriage** of specific bacterial strain increases **the risk of invasive diseases** leading to **Sepsis.**



References:
1.Bambang AW, Idrus I, Amin S, Iswanty M. Gonorrhea vaginitis in a pediatric patient: a case report. Pan African Medical Journal. 2021 Apr 14;38(1).
2.Thompson EC, Brantley D. Gonoccocal endocarditis. Journal of the National Medical Association. 1996 Jun;88(6):353.
3.Owusu M, Marfo KS, Acheampong G, Arthur A, Sarpong N, Im J, Mogeni OD, Annan A, Chiang HY, Kuo CH, Park SE. Gonococcal sepsis in a 32-year-old female: a case report. BMC Research Notes. 2018 Dec;11(1):1-3.

Case Report 6

Exceptional Diagnosis and Infection Control in Neonatal Sepsis Featuring a Rare Isolate - Wickerhamomyces anomalus

Authors : Dr. Sharanya R, Mr. Siby Jacob Kurian

Age/ Sex : **7-day-old preterm neonate** displaying clinical signs and symptoms indicative of sepsis, who was admitted to the Department of Pediatrics at Infant Jesus Hospital in Tirunelvelli.

Blood samples were collected using Bactalert blood culture bottles containing brain-heart infusion broth .These samples were subsequently sent to the Dept. of Microbiology at Microlab for culture and sensitivity analysis.

On the third day of incubation, the blood culture bottle yielded a positive result. The conventional identification methods, including culture on Blood Agar (BA) and Sabouraud Dextrose Agar (SDA), Gram staining, revealed spherical to ellipsoidal budding yeast cells with abundant pseudohyphae. These unidentified yeast-like fungal isolates were further identified through **MALDI-TOF MS** (Bruker Daltonics, Bremen, Germany) as **Wickerhamomyces anomalus**, with a confidence interval (CI) of 2.19.

A Pan-fungal test using Multiplex real-time PCR confirmed the presence of fungal infection in the patient. Subsequent blood samples collected within the next 5 days corroborated the possibility of infection. The patient received standard care throughout this period.

Notably, two other neonates within the department tested positive for Wickerhamomyces anomalus, indicating an outbreak situation. Numerous scientific studies, including those by Kalenic et al. (2001), Kalkanci et al. (2010), and Jung et al. (2018), have reported this species as a cause of outbreaks, especially among neonates, as documented by da Silva et al. (2013), Lin et al (2013), and Yang et al. (2021).

The pertinent information was promptly communicated to the treating pediatrician, and necessary infection control practices were swiftly implemented.

Wickerhamomycesanomalus, typically found in environmental sources such as soil, plants, and fruit juices (Ma et al., 2000), has infrequently been isolated from clinical specimens (Neumeister et al., 1992; Park et al., 2008; Ratcliffe et al., 2011). Recent studies, however, have underscored its clinical significance, implicating this species in various fungal infections, including keratitis, meningitis, and candidemia, often observed in immuno compromised and neonatal babies. (Neumeister et al., 1992; Park et al., 2008; Ratcliffe et al., 2011). Furthermore, Wickerhamomyces anomalus has been linked to a relatively high mortality rate of 41.2% (Pasqualotto et al., 2005). Studies have also identified it as a causative agent in hospital outbreaks (Kalenic et al., 2001; Kalkanci et al., 2010; Jung et al., 2018), particularly among neonates (da Silva et al., 2013; Lin et al., 2013; Yang et al., 2021).

Conclusion:

This case underscores the vital role of accurate microbiological diagnosis in **Neonatal Sepsis**, particularly when rare pathogens like **Wickerhamomyces anomalus** are involved. Timely identification facilitated tailored patient care and the prompt implementation of infection control measures, crucial in managing and preventing outbreaks within the healthcare setting. The evolving clinical significance of this uncommon pathogen underscores the need for ongoing research and heightened vigilance to safeguard vulnerable patient populations.

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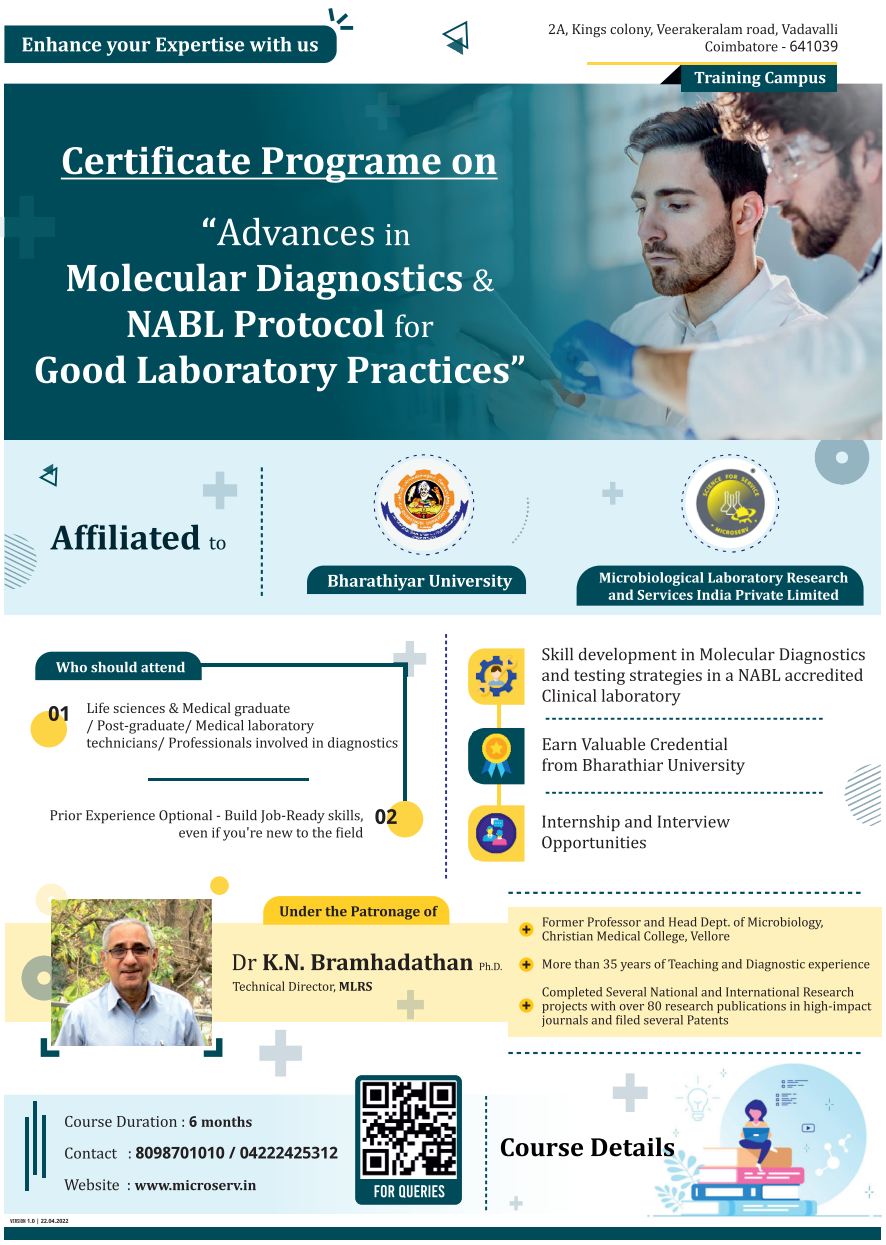

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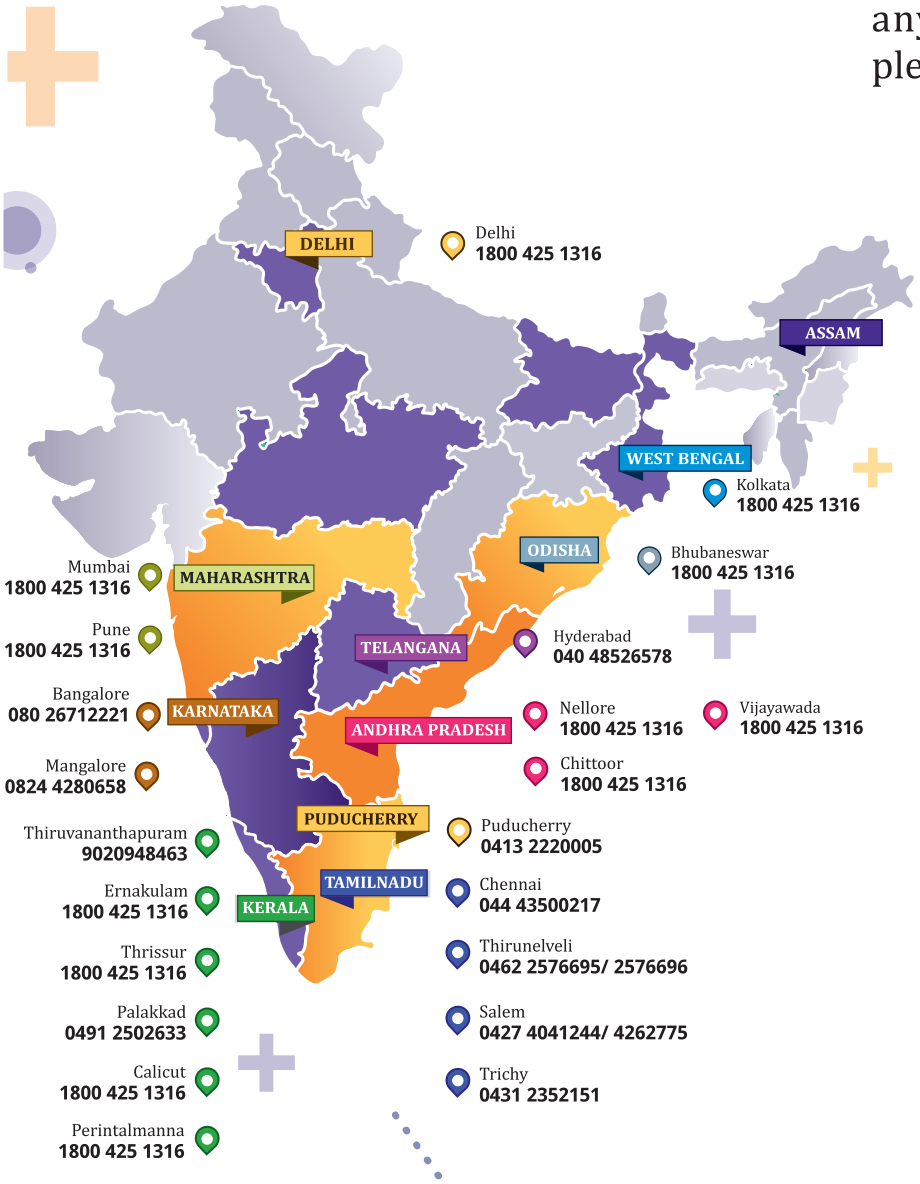

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