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RESEARCH ARTICLE

CHROMOBACTERIUM VIOLACIUM INDUCED UTI IN A FREQUENTLY RELAPSING NEPHROTIC SYNDROME: A CASE REPORT

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Abstract

A 9 year old boy with frequently relapsing nephrotic syndrome presented to paediatric department with complaints of periorbital oedema, decreased urine output, anorexia & abdominal pain. His vitals were stable with heavy proteinuria. He developed urinary tract infection by Chromobacterium violaceum. He was treated successfully with 1 gm% IV Ceftriaxone. Chromobacterium violaceum is a gram negative, oxidase positive, anaerobic, beta proteobacterium causing human infections infrequently. Found in tropical & subtropical regions as normal flora of water & soil. Around 150 cases of C violaceum was reported worldwide. Usually causes skin & soft tissue infections, visceral abscesses, meningitis, diarrhea, urinary tract infection, septicaemia etc. The organism is resistant to penicillin, narrow-spectrum cephalosporin, amoxicillin-clavulanic acid, polymyxin B & sensitive to fluoroquinolones, carbapenems, cotrimoxazole, chloramphenicol, aminoglycosides, etc. Delayed proper treatment due to limited awareness is responsible for high mortality rate. This case was reported for its rare clinical presentation being the first case to be described from a tertiary care centre of Arunachal Pradesh, North-East India.

Introduction:-

Recently ***Chromobacterium violaceum***, a rare entity has emerged as an important model of environmental opportunistic pathogen. Due to sparsity of cases, clinicians are unaware of rapid progression of infection & its unexpected antibiotic resistant pattern. This hinders to patient management. Formerly known as bacillus violaceum manilae. First identified by Bergonzini in 1881. Wooley in 1905, observed septicemia in infected water buffaloes and described it's pathogenic ability.[1,2] The first human case of ***C. violaceum*** infection was reported from Malaysia in 1927.

Since 1952-2009 comprehensive studies indicated 106 human cases of ***C. violaceum*** infection.[3] Updates from PubMed database on published clinical reports from 2010-2017, revealed that infections due to ***C. violaceum*** were still rare with its own significant mortality till date. Overall, there were less than 150 published clinical reports of human infections scatteredly found in Vietnam, Taiwan, Japan, United States, Brazil, Argentina, Australia, Senegal,

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Cuba, Nigeria, Singapore, & Sri Lanka.[4] A total 14 number of cases were documented from India, most of them were from southern & eastern part.[27]

It is saprophytic, non-pathogenic to human. Ubiquitously present in soil & fresh water. Well-known for producing violacein, a violet coloured pigment with antioxidant property.[6] Genus Chromobacterium consists of following nine species : ***C. subtsugae, C. aquaticum, C. haemolyticum, C. piscinae, C. pseudoviolaceum, C. vaccinii, C. amazonense, C. alkanivorans***, and ***C. rhizoryzae***. [7]

A gram negative, facultative anaerobic, beta proteobacterium, oxidase positive, motile, non-sporing, capsulated coccobacillus.[8] Usually causes skin and soft tissue infections, visceral abscess, meningitis, diarrhea, rarely UTI [9] and septicaemia if immunocompromised.Has high fatality rate of >50%. Better diagnostic facilities & improved antibiotic administrations can reduce mortality.[3]

There were no clinical trials evaluating different treatments. Due to rarity of clinical specimens, very limited antibiograms for this organism is available. After 1990, Ciprofloxacin & Carbapenems became predominant antimicrobial agents. Recently resistant to penicillins, narrow-spectrum cephalosporins, amoxicillin-clavulanic acid, polymyxin B and sensitive to fluoroquinolones, carbapenems, cotrimoxazole, chloramphenicol were reported.[10-16]

Here we presented a case of frequently relapsed steroid dependent nephrotic syndrome with urinary tract infection by ***C. violaceum***.

Case Report:

A 9 year old 29 kg male child was admitted to dept of paediatrics, TRIHMS with complaint of periorbital oedema since 6 days, decreased urine output since 3 days, anorexia & pain in abdomen for one day along with dental caries since 2-3 weeks. He was diagnosed as nephrotic syndrome with frequent relapse (Five episodes since last one year).

His vitals were stable , with mean temp 96.4˚F, PR-84 bpm, RR-26/min, SpO2-98%, mean BP-110/70 mm Hg, MAP-80.67.Bilateral pitting pedal oedema was present with no sign of pallor / lymphadenopathy / icterus / cyanosis /clubbing/nail changes. His respiratory, cardiovascular, gastrointestinal & central nervous system were within normal limit. Urine dipstick was suggestive of 3+ protein (proteinuria). Blood test showed normal Hb level (18.0 gm%), leucocytosis (TLC- 26.15 $X10^3/\mu l$) , altered Neutrophil/Lymphocyte ratio (N/L-78.7/14.3 & thrombocytosis. Liver function test showed hypobilirubinaemia with normal liver enzymes & hypoalbuminaemia. Renal function test was normal. Ophthalmology consultation was taken to rule out steroid toxicity features.

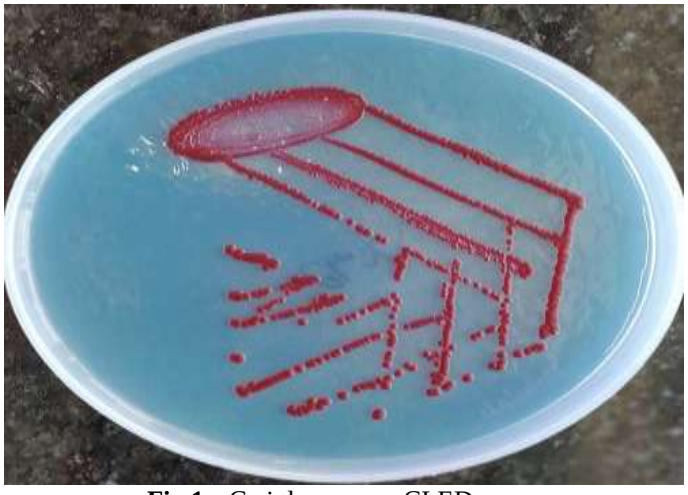

Fig 1:- C violaceum on CLED agar.

His urine sample was put on nutrient agar , blood agar , MacConkey and CLED agar for culture and incubated aerobically at 37℃ for 24 hours. Significant ($>10^5$ CFU/ml) growth of single type of smooth, round, glistening, with entire edge, convex, opaque, 2-3mm diameter, violet coloured non-diffusible pigmented colonies were found on

CLED agar, non-lactose fermenting colonies on MacConkey agar & non-haemolytic colonies on blood agar plate. Gram staining from pure isolated colonies showed gram negative organism.

Fig 2:- C violaceum on MacConkey agar.

Biochemical reactions interpreted it as (on table1) C violaceum.

Table 1:- Biochemical Tests Interpretation:

Sl No	Biochemical Tests	Results
1.	Gram stain	Negative
2.	Motility (Manitol motility agar)	Motile
3.	Oxidase	Positive
4.	Indole	Negative
5.	Triple Sugar Iron Test	
	Acid production in slant	Negative
	Acid production in butt	Positive
	Hydrogen sulphide production	Negative
	Gas production	Negative
	Glucose fermentation	Positive
	Lactose/Sucrose fermentation	Negative
	Alkali production in slant	Positive
6.	Citrate Utilisation Test	Positive
7.	Urea Hydrolysis Test	Positive
8.	Methyl Red Test	Negative
9.	Voges-Proskauer Test	Negative
10.	Oxidase	Positive
11.	O-F test	Both oxidative & fermentative
12.	Arginine dehydrolase	Positive
13.	Lysine decarboxylase	Positive
14.	Ornithine decarboxylase	Positive
15.	Pigment	Violet (violacein)

Antibiogram was done on Mueller-Hinton agar plate by Kirby-Bauer disk diffusion method. Result (Table 2) was interpreted according to Clinical & Laboratory Standards Institute (CLSI) guidelines for non-Enterobacteriaceae Gram-negative bacteria.The algorithm of diagnosing C. violaceum was given on fig3.

Table 2:- Antimicrobial Susceptibility Pattern.

Antimicrobial Agents	Interpretations	Antimicrobial Agents	Interpretations
Amikacin (AK)	Sensitive (S)	**Gentamycin (GEN)**	Sensitive (S)
Cefazolin (CAZ)	Resistant (R)	**High Level Genta (HLG)**	Sensitive (S)
Clindamycin (CD)	Resistant (R)	**Imipenem (IPM)**	Resistant (R)
Ciprofloxacin (CIP)	Resistant (R)	**Levofloxacin (LE)**	Sensitive (S)
Colistin (CL)	Sensitive (S)	**Linezolid (Lz)**	Resistant (R)
Cefepime (CPM)	Sensitive (S)	**Meropenem (MRP)**	Resistant (R)
Ceftriaxone (CTR)	Sensitive (S)	**Nitrofurantoin (NIT)**	Resistant (R)
Cotrimoxazole (COT)	Sensitive (S)	**Erythromycin (E)**	Resistant (R)
Cefoxitin (Cx)	Resistant (R)	**Novobiocin (Nv)**	Resistant (R)
Doxycycline (DO)	Resistant (R)	**Piperacillin-Tazobactam (PIT)**	Sensitive (S)
Doripenem (DOR)	Sensitive (S)	**Vancomycin (VA)**	Resistant (R)

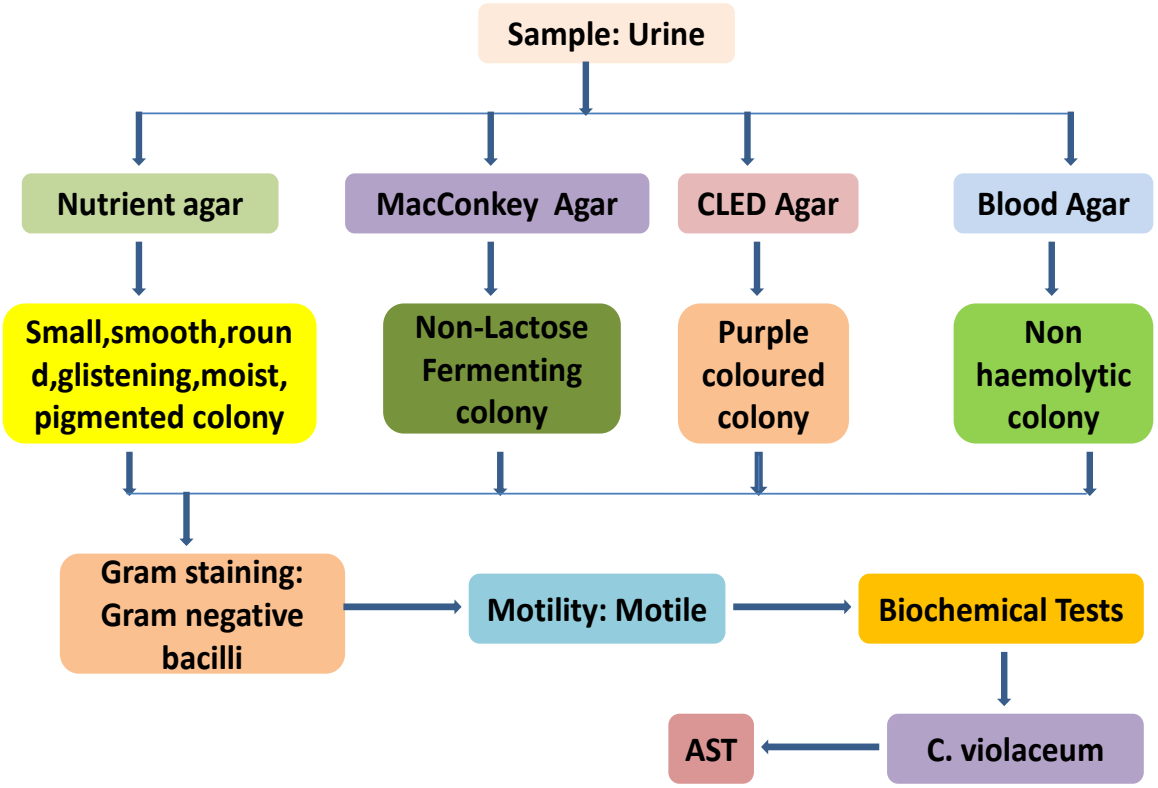

Fig3: Algorithm of Diagnosing C. violaceum

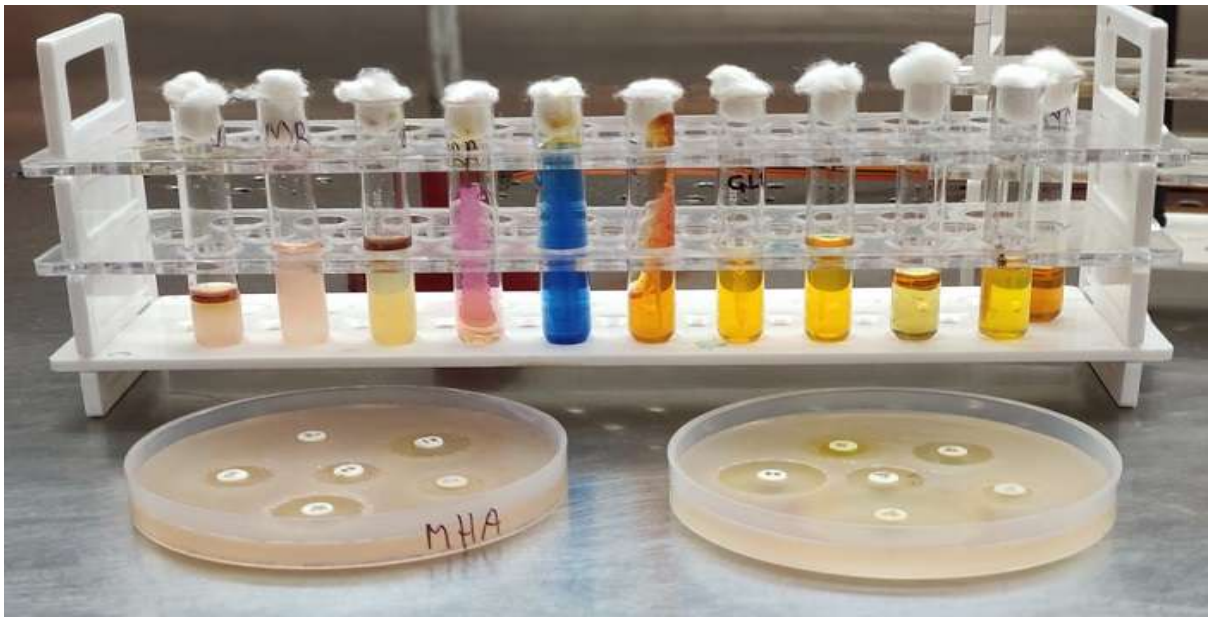

Fig 4:- Biochemical panel of C violaceum.

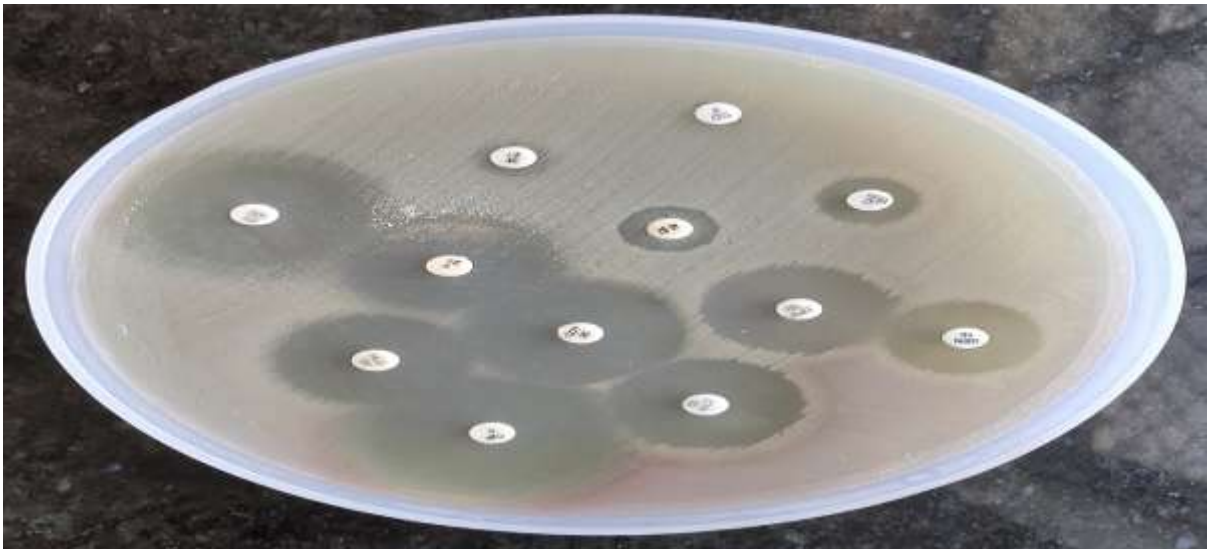

Fig 5:- Antimicrobial susceptibility testing of C violaceium.

He was treated with IV Ceftriaxone 1 gm % 12 hourly along with other drugs. He was discharged under haemodynamically stable condition.

Discussion:-

The scarcity of reports of human infections with ***Chromobacterium violaceum*** is hindrance in patient's management and so limits of awareness of clinicians. Being mesophilic, prefer growing at temperature between 20°C and 37°C, in tropical & subtropical areas & in summer month. Here we attended a patient from rural area & temperate climate in month of September. No age predilection was reported in literature.[17] There were reported UTI cases in 11 month old, 2.5 years [18] ,19 years [9] ,36 years [19] & 70 years [20] old person. Predominant in male. Route of entry is transcutaneous following trauma & oral during ingestion of contaminated water & seafood. Commonest route found in literature is following encatheterisation or surgery. No such history present here. Clinically manifested as pneumonia, gastrointestinal tract infections, urinary tract infections, localised cutaneous lesions, localised or metastatic abscesses, osteomyelitis, meningitis, peritonitis, endocarditis, hemophagocytic syndrome, respiratory distress syndrome, and fulminant sepsis etc [12,21,22,] This is an unusual case of frequently relapsing nephrotic

syndrome with urinary tract infection. To the best of our knowledge, this is the first case of C. violaceum infection in tertiary care hospital, Arunachal Pradesh.

It is considered as a low virulence bacterium infection in immunocompromised patients. Mirror image of immunocompromised state revealed here. Patient is treated with long acting steroid, tab prednisolone 55 mg (30+20+5) OD. Sepsis due to chromobacterium may mimic melioidosis, in melioidosis endemic areas. Usually identified by conventional biochemical reactions, VITEK 2 Compact System, PCR.[23] Here we used conventional biochemical reactions for identification.

In our case the following points favoured the diagnosis: history of nephrotic syndrome with compromised immune system, frequent relapse, under steroid treatment. Isolation of single type of pure colony with colony count 10^5/ml on culture of urine sample & then repeated isolation of same organism on culture. Sensitive to aminolycosides, 3rd,4th,5th generation cephalosporins, fluoroquinolones and resistant to 1st & 2nd generation cephalosporin, macrolids. Most strains showed resistant to penicillins and other beta-lactam antibiotics and, indeed, increased level of beta-lactamase [24,25,26].Ciprofloxacin is the most effective antibiotic in vitro. It is also susceptible to Gentamicin and Amikacin. This coinsides with our study. With combined antimicrobial therapy we can get better prognosis.

Conclusion:-

Urinary tract infection due to C. violaceum is an emerging trend. If not treated well in appropriate time & sequence with proper dose schedule may lead to fatal sepsis. Inadequate knowledge about pathogenesis & antimicrobial resistant pattern of this bacterium is a challenge to be tackled.Here need of awareness of physicians in tropical & subtropical regions to render effective treatment course to get rid of C violaceum infection.

Conflict of Interest:

The authors declare that there is no conflict of interests regarding the publication of this paper.

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