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RESEARCH ARTICLE

SEPTICEMIA DUE TOGLOBICATELLA SANGUINIS IN AN IMMUNOCOMPETENT ADULT: A CASE REPORT ANDLITERATURE REVIEW

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Abstract

Background: Globicatella Sanguinis is a germ that is rarely isolated in practice; however, in view of identification errors due to its resemblance to viridans streptococci and the difficulties presented by many commercial systems of phenotypic identification, this pathogen remains underappreciated. Several works have highlighted the isolation of this bacteria, but the clinical characteristics and modes of infestation are still unknown.

Case presentation:A 82-year-old Moroccan woman with high blood pressure and type 2 diabetes was discovered unconscious and transferred to our unit for medical care. He was immunocompetent with no history of malignancies, recurrent infections or immunosuppression medications. The investigation of the febrile consciousness disorder presented by the patient reveled Globicatella sanguinis in blood cultures. All other septic simples were negative. The evolution was marked by apyrexia, and an improvement in her state of awareness after rehydration, antimicrobial medication, glycemic and blood pressure rebalancing.

Conclusions: This is the first case of Globicatella sanguinis isolation in our department. Literature review shows a high MIC level against third generation cephalosporins. In light of the increasing emergence of drug-resistant bacteria, the establishment of appropriate antibiotics has become an imperative necessity. However, more researches are required to look into the pathophysiology and risk factors of G. sanguinis infections among humans. Its low occurrence may be attributable in part to difficulties in laboratory identification, and it is probable that recognition of this organism will improve when modern technologies such as MALDI-TOF MS and next-generation sequencing become more widely used.

Introduction:-

Globicatella sanguinis (G. sanguinis) is a rare pathogenic Gram-positive coccus that has been sporadically reported as an unusual cause of human infections. Multiple studies suggest that G. Sanguinus can colonize inguinal skin (1),

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and elderly female patients with a history of cerebrovascular disease are more susceptible to this infection. (2)However, the epidemiology and the clinical significance of this pathogen remain largely unknown. G. sanguinis is an unusual pathogen that could be misidentified or misdiagnosed with viridans streptococci due to its colonial morphology despite its unusual antimicrobial susceptibility pattern(3). We report another case of the rarely isolated G. sanguinis bacteremia with a literature review of published cases until August 2022.

Casepresentation

Mrs. RH, 82, lives alone in an apartment and has had high blood pressure for 22 years on a calcium channel blocker and type 2 diabetes for 24 years on metformin, without any other medical or surgical past history. The patient was found unconscious at her home and was transferred to our facility for further medical care.

On admission, the patient was unconscious with a Glasgow coma scale of 10/15 and a capillary blood glucose of 2.1g/l, with no asymmetry of motor response, a fever of 39°C, rales on auscultation, edema of the lower limbs, and diffuse tenderness on abdominal palpation.

Following a series of blood cultures, ceftriaxone was administered, and an urgent cerebral CT scanwith contrast injection was performed, which revealed no abnormalities. As the patient presented with fever and altered mental status, we performed a lumbar puncture, urinalysis and urine culture, chest x-ray, abdominal ultrasound and CT scan with contrast injection, as well as a complete blood count with differential. Results showed leukocytosis with neutrophilic predominance (14.59 X 103) and an elevated C-reactive protein at 25.87. The analysis of cerebrospinal fluid, urine, and ascitic fluid was unremarkable, and the cultures were sterile.

Apart from abdominal tenderness on physical examination and ascites on abdominal imaging, no infectious entry point has been objectified. Probabilistic antibiotic therapy based on ceftriaxone, metronidazole, and gentamycin was initiated; all medications were tailored to renal function.

The blood cultures were positive after 48 hours of incubation, showing alpha hemolytic colonies, appeared on blood agar incubated under aerobic condition at 37°C with 5% CO2. Similar colonies were also observed on Chocolate agar plate. It was catalase negative and showed no zone of inhibition around a 5µg disc of optochin. The agglutination test for pneumococci was negative. It was presumptively identified as viridans streptococci. For bacterial identification MALDI-TOF MS was performed which confirmed the identity of Globicatella sanguinis. table 1 summarizes the results of the antibiogram.

Table 1:- Results of the antibiogram.

Antimicrobial Agent	**Interpretation**
Penicillin G	Sensitive
Ampicillin	Sensitive
Amoxicillin	Sensitive
Vancomycin	Sensitive
Moxifloxacin	Sensitive
Levofloxacin	Sensitive

The patient's evolution was marked by apyrexia, and an improvement in her state of awareness after rehydration, antimicrobial medication, glycemic and blood pressure rebalancing.

Our patient was immunocompetent with no history of malignancies, recurrent infections or immunosuppression medications. Also, she was tested negative for HIV infection.

Discussion:-

Literature Review:-

A search for all published medical literature available on PubMed and Google Scholar including the keyword "globicatella". Searches involved all published papers till August 2022, concerning infections due to Globicatella Sanguinis. In a second time the results collected have been revisited and rescreened in order to eliminate duplicate works and those concerning infections for other species than humans.Then we shared another case of G. sanguinis bacteremia that was isolated in our unit.

Our search matched 157 paper, after excluding duplicate results and publications concerning species other than humans, our review included 52 works, associated to our case report it's a total of 53 human cases of Globicatella Sanguinis infection (figure 1)

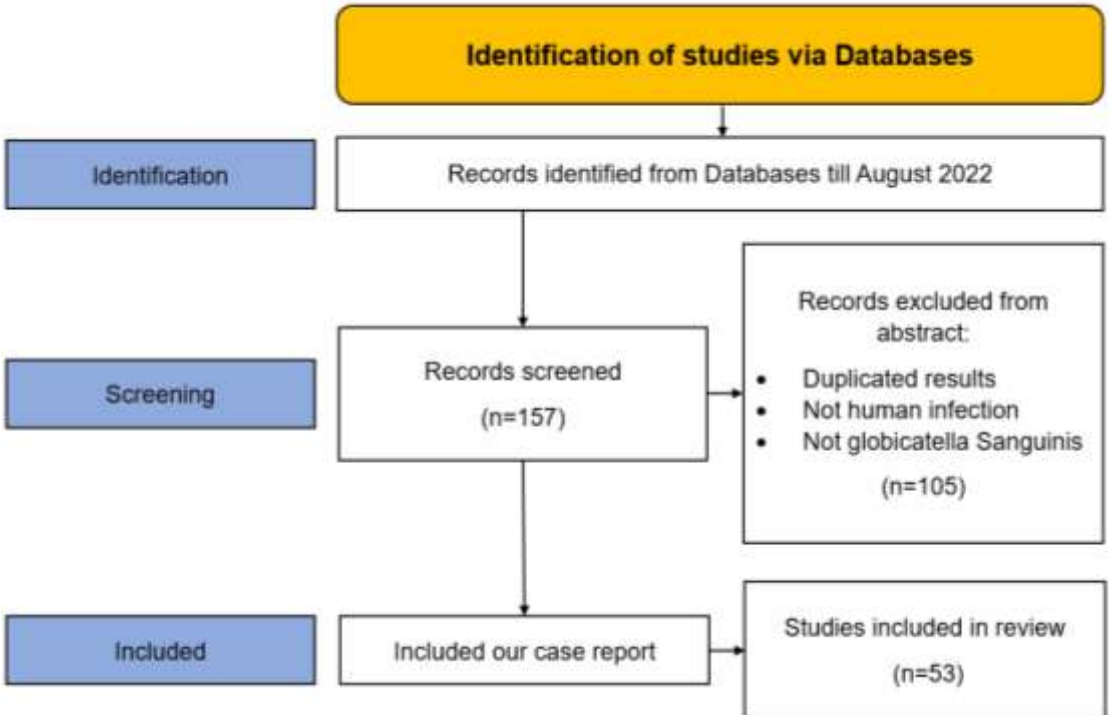

Figure 1:- Flowchart summarizing the results of the literature search.

Globicatella sanguinis has been linked to different infections. Table 2 summarizes the complete published clinical experiences with Globicatella infections (53 patients).

Table 2:- Review of published cases of Globicatella Sanguinis human infections.

Publication	Country	Age	Gender	Underlying conditions	Signs and symptoms	Site of isolation	Infection / diagnosis
This publication	Morocco	82	F	High blood pressure and type 2 diabetes	Febrile consciousness disturbances	Blood	Bacteremia
(1)	France	56	F	Nd	Vomiting and headache, associated with instability when walking, memory impairment, and clinical signs of meningitis	CSF	Meningitis
(4)	Japan	94	M	Dementia, hypertension, hyperlipidemia, and osteoporosis	Back pain and fever	Urines and blood	UTI
(5)	Germany	69	M	Normal-pressure hydrocephalus, depressive disorders	Clinical signs of meningitis	CSF	**I.** ME NINGITIS
(6)	India	70	M	Traumatic temporo-parieto-occipital hematoma, decompressive craniectomy with evacuation of the hematoma and	High-grade fever, heavy purulent discharge from the wound at the surgical site on the scalp and unconsciousness	CSF	Meningitis

				contusectomy			
(7)	Denmark	23	F	History of intravenous heroin and cocaine abuse, right-sided endocarditis, and hepatitis C	Fever (39.58°C), mild dyspnea and right-sided thoracic pain	Blood	Pneumonia
(7)	Denmark	82	F	History of Alzheimer's disease and hypertension	Dehydration and suspicion of urosepticaemia	Blood	Bacteremia
(7)	Denmark	56	M	History of Crohn's disease and atrial fibrillation	Body temperature was 37.98C. The right arm was red, warm with oedema	Blood	Erysipelas
(2)	Japan	87	F	Recurrent episode of UTI, subarachnoid hemorrhage, surgical construction of ventriculo-peritoneal shunt, and gastrostomy	A fever for 5 days, hematuria despite taking oral levofloxacin and acetaminophen, Glasgow Coma Scale (GCS) of 7 and blood hypotension	Blood	Endocarditis
(8)	China	80	F	Diabetes mellitis, hypertension, and gouty arthritis	Chronic diarrhea, hypercalcemia, sudden cardiac arrest 2 weeks after admission	Blood	Bacteremia
(8)	China	92	F	Dementia, congestive heart failure, and history of recurrent urinary tract infection	Fever and productive cough	Blood	Bacteremia
(9)	India	9	M	Head trauma	N/A	Pus	Corneal abscess with endop-hthalmitis
(10)	Korea	76	F	Hypertension and rheumatoid arthritis	Surgical site pain (total left knee replacement)	Blood	Surgical site infection
(11)	Turkey	43	F	Hypertension and chronic renal failure due to diabetic nephropathy, coronary stent holder	Chills, fever, and hemodialysis catheter dysfunction	Blood	Femoral hemodialysis catheter-related bacteremia
(12)	Turkey	39	F	Lumbo-peritoneal shunt	Neck stiffness, fever, and tachycardia	CSF	Meningitis
(13)	USA	63	F	Mixed myelodysplastic and myeloproliferative disease on Hydroxyurea, chronic renal insufficiency, and obstructive uropathy status post bilateral ureteral stent placement	Nausea, vomiting, diaphoresis, fatigue, slurred speech and diplopia	CSF	*A.* Meningoencephalitis and acute brain abscesses
(14)	Colombia	1	F	Fenestration of the floor of the third ventricle for hydrocephalus	febrile intracranial hypertension	CSF	Meningitis

(15)	Morocco	5 months	F	Known posterior fossa tumor	Fever, vomiting, seizures and refusal to feed	CSF	Meningitis
(16)	USA	ND	N/A	N/A	N/A	Pus	Wound infection
(16)	USA	ND	N/A	N/A	N/A	Pus	Ear abscess
(17)	India	1 month	N/A	N/A	N/A	CSF	Meningitis
(18)	USA	64	F	Hight blood pressure	Seizures and encephalopathy	Blood	Septic shock
(19)		70	F	End stage renal disease, initiated on hemodialysis by ash catheter	Shortness of breath, fatigue, and loss of appetite for two weeks, fever and TSV	Blood	Bacteremia
(20)	USA	72	F	Obesity, gastric lap banding, tobacco	Hip pain	Hip synoviu m	Prosthetic joint infection
(20)	USA	54	F	Obesity, diabetes mellitus, gastric bypass, tobacco	Fatigue and fever	Blood	Bacteremia
(3)	USA	N/A	F	N/A	N/A	Blood	Bacteremia
(3)	USA	N/A	F	N/A	N/A	Blood	Bacteremia
(3)	USA	N/A	M	N/A	N/A	Urine	UTI
(3)	USA	N/A	N/A	N/A	N/A	Blood	Bacteremia
(3)	USA	N/A	N/A	N/A	N/A	Blood	N/A
(3)	USA	69	M	N/A	N/A	Urine	UTI
(3)	USA	85	F	N/A	N/A	Urine	UTI
(3)	USA	N/A	N/A	N/A	N/A	Blood	N/A
(3)	USA	1	M	N/A	N/A	CSF	Meningitis
(3)	USA	84	F	N/A	N/A	Blood	Bacteremia
(3)	Canada	N/A	F	N/A	N/A	Urine	N/A
(3)	USA	90	F	N/A	N/A	Blood	UTI
(3)	USA	68	F	N/A	N/A	Blood	N/A
(3)	Canada	82	F	N/A	N/A	Blood	N/A
(3)	Canada	79	F	N/A	N/A	Blood	N/A
(3)	USA	N/A	N/A	N/A	N/A	Blood	N/A
(3)	USA	1	M	N/A	N/A	Blood	Bacteremia
(3)	USA	N/A	N/A	N/A	N/A	Blood	N/A
(3)	USA	58	M	N/A	N/A	Blood	Bacteremia
(3)	USA	82	F	N/A	N/A	Blood	Bacteremia
(3)	Canada	2	F	N/A	N/A	Blood	N/A
(3)	Canada	92	F	N/A	N/A	Blood	N/A
(3)	Canada	N/A	F	N/A	N/A	Blood	N/A
(3)	USA	70	F	N/A	N/A	Blood	Endocarditi s
(3)	Canada	43	F	N/A	N/A	CSF	N/A
(3)	Canada	85	M	N/A	N/A	Blood	N/A
(3)	Canada	1	F	N/A	N/A	Blood	N/A
(3)	USA	3	F	N/A	N/A	Blood	Bacteremia

UTI: urinary tract infection; N/A: not available; CSF: cerebrospinal fluid; M: male; F: female

Analyzing the published clinical experiences with Globicatella infections, 75.55% of patients were female, and a majority of patients were either older than 65 (53.66%) or younger than 5 years (19.51%), with an average age of 55.54 (+/- 32.09). Of these 53 reported human cases of G sanguinis, 15 presented with bacteremia (73%), nine with CNS infections, five with urinary tract infection, other sporadic infections were more rarely reported such as two patients who had a surgical site infection, two patients presented endocarditis, one case of pneumonia, one had erysipelas, one had ear abscess, one had eye abscess with endophthalmitis, one case of joint infection and one patient presented a catheter related bacteremia.

However, co-infections with other pathogen agents were objective in 3 cases with Corynebacterium riegelii, Pseudomonas aeruginosa, Streptococcus sanguisand Trueperellabernardiae. Eight cases occurred in a perioperative context, mainly neurosurgical intervention (six of eight cases).

No obvious association between infection site and age or gender was apparent. To our knowledge, this is the first documented case in our unit and the second in Africa.

Discussion:-

Several strains of uncertain taxonomic position were identified during a study of Gram-positive catalase-negative cocci from human clinical sources, leading Collins et al. to identify a new genus and species, **G sanguinis** (21), which has been linked to human septicemia, meningitis, endocarditis, and urinary tract infection. **G sulfidifaciens**, a second species linked to cattle illnesses, was later identified (22). Although this species has not been linked to human diseases, it has been shown to colonize human skin surfaces (1).

The two species of the genus **Globicatella** are Gram-positive cocci that are aerobic, -hemolytic, catalase-negative, PYR-negative, and belong to the Firmicutes phylum and the **Aerococcaceae** family (23).

The rare reports of **Globicatella** species isolation from humans have only concerned cases of **G. sanguinis** infection.

Globicatella forms chains of tiny hemolytic Gram-positive cocci colonies. Certain features can contribute to the differentiation of **Globicatellaspp** and **viridans group streptococci**, for instance, biochemical tests that can help in the identification of this pathogen include negative leucine aminopeptidase reaction (LAP) and growth in the presence of 6.5% NaCl. The viridans streptococci are pyrridonylarylamidase (PYR) negative and LAP positive, and, do not grow in the presence of 6.5% NaCl (21,23).

Commercial phenotypic identification systems have difficulty distinguishing **G sanguinis** from other **streptococci** (3). In fact, there exist various descriptions of biochemical reactions for the same species. Standardized techniques, such as Rapid ID 32 STREP or API 20 STREP, are known to detect **alpha haemolytic streptococci** (24), but they were not accessible in our settings. The MALDI-TOF MS was used to determine the identity of **G. sanguinis** in our patient. Mass spectrometry has the potential to be an effective method for identifying catalase negative gram-positive cocci, especially in species with complicated diagnosis (25).

Shewmaker and colleagues (3) reported the first antimicrobial susceptibility testing results of 27 clinical **G. sanguinis** samples. Only one sample was resistant to levofloxacin in this investigation, and all strains were sensitive to vancomycin and amoxicillin. The results of the other antimicrobials (chloramphenicol, erythromycin, tetracycline, and clindamycin) were variable.

As the prevalence of drug-resistant bacteria rises, reliable identification of drug-resistant strains has become critical. Because of their strong likeness, previous findings of antibiotic susceptibilities of **viridans streptococci** may have included some **G. sanguinis** strains. Because this bacterium has demonstrated some intermediate resistance to penicillin, it is crucial to identify and monitor antibiotic resistance in this organism (6).

Given that there is no Clinical and Laboratory Standards Institute (CLSI) approval interpretation guideline for Globicatella, the laboratory should only report minimum inhibitory concentrations (MIC). In cases of other

Globicatella infections, antibiotic susceptibility was determined using the viridans group Streptococcus spp. criteria. According to **Shewmaker** et al., resistance rates to cefuroxime, cefotaxime, and meropenem were as high as 74%, 48%, and 37%, respectively, in contrast to 100% susceptibility to penicillin and amoxicillin. After using -lactam-based antibiotics and macrolides as an empirical regimen, G. sanguinis developed resistance to both antibiotics, which was linked to a decrease in bacteremic pneumococcal pneumonia mortality.

It is difficult to explain why the majority of **G. sanguinis** infections, including this one, were discovered in elderly female patients. **G. sanguinis** would infect livestock and farmers (1), but the exact mode of infection was unknown. **G. sanguinis** typically had a high MIC level against third generation cephalosporins (20), which were commonly employed as empirical antibiotics, but a low MIC level against penicillin. Treatment requires early and accurate detection of G. sanguinis infection.

Conclusions:-

The establishment of appropriate antibiotics has turned into an absolute necessity due to the rising prevalence of germs that are resistant to common antibiotics. This can be achieved by correctly identifying clinical infections and treating them based on sensitivity patterns. However, more research is required to look into the pathophysiology and risk factors of **G. sanguinis** infections among humans. Its low occurrence may be attributable in part to difficulties in laboratory identification using phenotypic approaches, and it is probable that recognition of this organism will improve when modern technologies such as MALDI-TOF MS and next-generation sequencing become more widely used.

More case reports may emerge as patients suffering from severe immunosuppression survive longer. Globicatella sanguinis should be considered as an opportunistic agent for many infectious conditions.

Abbreviations:

MIC: minimum inhibitory concentrations
G. sanguinis: Globicatella sanguinis
CT: Computed tomography
HIV: human immunodeficiency viruses
CNS: Central Nervous System
PYR: PyrrolidonylArylamidase
LAP: leucine aminopeptidase reaction
CLSI: Clinical and Laboratory Standards Institute

Declaration section

1. **Declaration of conflicting interests**

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

2. **Ethics Approval and consent to participate**

Not applicable.

3. **Consent for Publication**

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

4. **Availability of supporting data**

All clinical finding and biological results included in this case report can be found in the archived medical file of the patient.

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Authors' contributions
All authors have contributed to this work since conception, reading and endorsing the final version of the manuscript.

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