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Infective Endocarditis and Pulmonary Septic Emboli with secondary Catastrophic antiphospholipid syndrome (CAPS) in a case of Rat bite fever.

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ABSTRACT

Catastrophic antiphospholipid syndrome (CAPS) is a rare and life-threatening disease[3]. It is characterized by multiple arterial and/or venous thrombotic events, including the microcirculation, occurring in a short period and can affect any system[5]. Catastrophic antiphospholipid syndrome can occur in individuals with known Anti-phospholipid syndrome(APS) under treatment, or it can be its first manifestation[6]; In most cases, there is a triggering factor that can be identified.

Rat bite fever is an underdiagnosed illness and endocarditis is one of its rare complication[6]. We report a case of Rat bite fever with endocarditis with CAPS with multiple thromboses at unusual sites, including the lungs, liver, spleen, pectineus muscles, heart and kidney, in a previously normal 8-year-old boy.

I. INTRODUCTION

Catastrophic antiphospholipid syndrome (CAPS) is characterized by multiple arterial and/or venous thrombotic events occurring in any organ system over a short period[1]. Catastrophic antiphospholipid syndrome may develop in individuals with previously diagnosed APS, or it may present as the first manifestation of APS[2].

The prevalence of CAPS is currently estimated to be 1%, with a mortality rate of 37%[6]. In most cases, a triggering event can be identified including infection, withdrawal of (or subtherapeutic levels of) anticoagulationand coexistence of systemic lupus erythematosus (SLE) flare[14]. When CAPS is suspected, prompt initiation of treatment in the intensive care setting is crucial for an optimal outcome[7].

Infective endocarditis (IE) is a relatively uncommon condition in children but it causes significant morbidity and mortality[19]. Repaired and unrepaired congenital heart disease are associated with a high lifetime risk of infective endocarditis; patients with ventricular septal defect have the highest risk.[15] Acute tricuspid valve endocarditis is rare and usually associated with habitual intravenous self-administration of drugs and more often is associated with central line infections.[9]

Septic pulmonary embolism is an uncommon occurrence in children[9]. Numerous pulmonary infarcts resulting from small emboli may be associated with right-sided bacterial endocarditis, septic thrombophlebitis, and osteomyelitis [3]. Moreover, coexistence of both infective endocarditis and septic emboli is very rare. We present here a child with both Infective endocarditis and septic emboli due to a very rare etiology and a case of CAPS induced by infection (probable rat bite fever) where multiple thrombotic events occurred at unusual sites.

II. CASE REPORT

A previously healthy 8-year-old boy presented to the paediatrics emergency department with a 4-day history of fever, headache,body ache and increased respiratory activity. He had history of rat bite on left foot 2days prior to fever. On physical examination he was ill-looking and febrile, heart rate was 140 beats/min, blood pressure was 98/60 mmHg, air room saturation was 95–97%, and body weight was 26 kg (50th percentile). His physical examination revealed pallor, petechial rash+ over soles of legs, with liver palpable 2cm and decreased air entry to both lungs and a 2/6 grade systolic murmur. Laboratory analysis showed microcytic anemia with hemoglobin 6.8 g/dL, a white cell count 16.4 × 10^3/μL, and platelets 0.41 ×10^3/μL. Erythrocyte sedimentation rate was 40 mm/hr. Liver and kidney function tests were normal. Dengue,malaria,widal tests were negative. Urine analysis revealed slight leukocyturia of 10 cells/μL; single blood culture was negative. Chest X-ray showed infiltrates in left lower lobe, cardiomegaly and paratracheal widening; Urine culture result was sterile. The boy was started on symptomatic management. The

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child was given doxycycline and inection Crystalline Penicillin as rat bite fever was suspected.

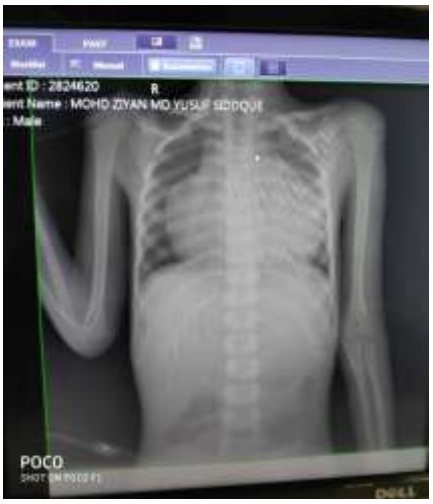

Figure 1
cardiomegaly.

Two days after his admission echocardiography was done and revealed 10 vegetations attached to the mitral valve with a mild eccentric mitral regurgitation without other valvular abnormalities (Figures 2, 3, and 4) with 2 vegetations in RVOT with moderate pericardial effusion with good LV function. No ventricular septal defect or patent foramen ovale was demonstrated. Intravenous Gentamicin, and Vancomycin were administered in view of multiple vegetations. Ophthalmologic examination was normal and no other immunologic signs of infective endocarditis were noticed. Investigations included peripheral blood smear; dsDNA,ASO, CRP; ANA and throat swab; . All these tests were negative and five blood cultures were sterile.

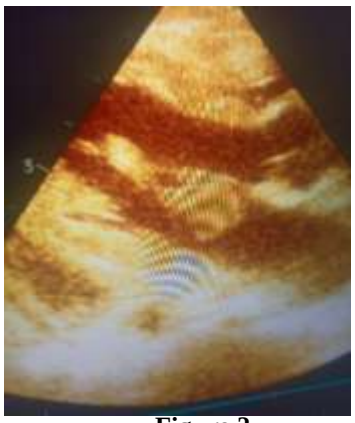

Figure 2
Mitral leaflet vegetations.

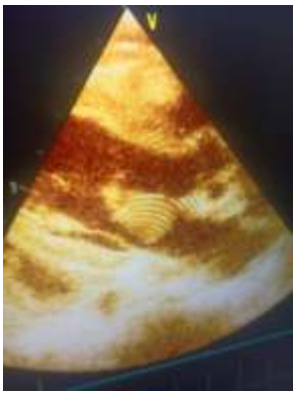

Figure 3
2DECHO showing mitral vegetations

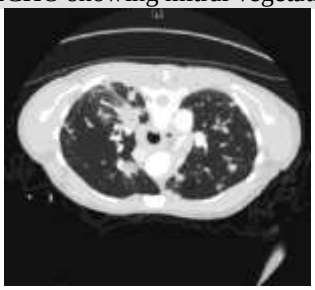

Figure 4
Septic emboli in the bilateral lower pulmonary segments.

Urgent CT scan was done to look for thrombosis elsewhere- CECT thorax showed multiple variable sized intrapulmonary nodules withcavitations in bilateral lung fields sparing right middle lobe likely suggestive of pulmonary septic emboli. CT abdomen showed bilateral renal lower pole infarct (right>left), multiple splenic infarcts,mild ascites, with bilateral mild hip joint effusion and forming abscess in right pectineus muscle. Repeat three blood cultures were again negative (blood cultures at our institute are routinely cultured for 7 days). **Initial cardiolipin antibody and beta 2 glycoprotein were negative but repeat sent after 2 weeks due to deterioration of the child werepositive (cardiolipin IgM positive and beta 2 glycoprotein IgM positive).**

A senior rheumatologist was consulted and the child was diagnosed with probable catastrophic APLA secondary to probable rat bite fever hence was started on heparin and high dose IV steroids and IVIg. Plasmapheresis was planned for the child but the child developed subsequent pulseless electrical activity , cardiac arrest and passes away.**Final blood culture after 4 weeks of incubation showed methicillin resistant staph aureus.**

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III. DISCUSSION

We report the case of a young boy who was initially reported to be healthy with no congenital heart disease who developed mitral infective endocarditis with septic emboli due to a rare etiology,Streptobacillus monoliformis with secondary APLA syndrome.

Our patient was diagnosed with infective endocarditis based on modified Duke Criteria [17]. The presented boy had one major criterion, which was evidence of endocarditis on echocardiography (mitral vegetation and mitral regurgitation) along with three minor criteria: (1) blood culture suggestive of MRSA (2) fever, and (3) pulmonary emboli.

Infective endocarditis in children with congestive heart disease can potentially lead to major complications in and outside the heart[9]. Congestive heart failure occurs in up to 40% of cases and is the leading cause of hemodynamic compromise; this could be due to many factors including the destruction of valves, myocarditis, or arrhythmias[11]. Extracardiac complications are also frequent in up to 43% of cases and are caused by either embolic events or immune phenomena. Vegetation on the mitral valve has a high risk of resulting in septic pulmonary emboli, causing various pulmonary complications such as pneumonia and pulmonary abscess[3]. Our patient had developed septic pulmonary emboli originating from the mitral vegetations.

Repeated blood cultures taken at his presentation did not grow any pathogen and during the course of hospitalization did grow MRSA. According to literature, the rate of culture-negative endocarditis varies with different studies, ranging from 2.5% to 31% [4].

Rat bite fever is a systemic zoonotic disease caused by infection with either S. moniliformis or Spirillum minus, both gram negative bacilli.[15] Rat bite fever encompasses 2 different disease syndromes dependent on the causative organism-S.monoliformis and Spirilliumminus.Geographically ,S.monoliformis is more commonly found in North America and Europe whereas Spirillum minus (also known as Sudoku) has been reported more frequently in Asia[16]. Case reports are almost exclusively secondary to S. moniliformis, probably because S. moniliformis is easier to isolate in the laboratory with current automated culture systems. Streptobacillus is a fastidious, pleomorphic, non-capsulated , non-motile gram negative bacillus found in the nasopharynx and oropharynx of rodents[9]. Human infection can result from a bite or scratch from an infected or colonized rat or consumption of contaminated food or water. Children, pet owners, pet shop and animal research laboratory workers are more susceptible to infection[11].

Ratbite fever is an underdiagnosed febrile illness characterised by fever, myalgias, arthralgias/arthritis, vomiting, headache and rash[12]. Many serious complications reported include meningitis, pericardial effusion, endocarditis and multiple organ failure. The case-fatality rate is as high as 25% in untreated patients. S. minus infection is differentiated from S. moniliformis infection by the following: a longer incubation period, intermittent/recurrent fever, large macular or papular rash, arthritis is rare, blood cultures are usually negative and the organism is seen on a dark field blood smear preparation[13]. Broad-range PCR amplification of parts of the 16S rRNA genes followed by sequencing has also been demonstrated to identify this organism.[13]

Endocarditis is a rare complication of Streptobacillus monoliformis bacteremia with only 22 cases having being published since 1915 and even fewer with embolic phenomenon.. Majority of cases reported had underlying valvular abnormalities, prosthetic valve or rarely congenital heart disease.[13-14]

Native valve endocarditis is extremely unusual. For Rat bite fever intravenous penicillin followed by oral penicillin or ampicillin is usually recommended[11]. In patients with penicillin allergy, alternatively tetracycline or doxycycline is used. In patients with infective endocarditis crystalline penicillin for 4 weeks plus gentamicin for 2 weeks have usually been used. In patients sensitive to penicillin, vancomycin with gentamicin can be used.[10]Aminoglycosides enhance activity against the cell wall deficient L forms of S. moniliformis. There has been one previous case report of RBF with endocarditis from India. Poor culture techniques and empiric antibiotics may result in under-reporting of this condition.In the majority of cases reported, the clinical presentation may be nonspecific with fever, rashes, polyarthritis and murmur, which can mimic acute rheumatic carditis or culture negative endocarditis.[13] However, a history of rat bite, positive echo/TEE for vegetations and positive blood culture for S. moniliformis or a positive PCR (16S rRNA gene) can confirm the diagnosis.

Catastrophic antiphospholipid syndrome is the most severe form of APS with life threatening mutliorgan involvement developing over a short period of time,usually associated with microthromboses. [6]

The unique characteristics of CAPS are:

1. Rapid onset thromboses resulting in MODS(multiorgan dysfunction syndrome).
2. Common associations with other thrombotic microangiopathies(TMA's)
3. Evidence of systemic inflammatory response syndrome
4. High risk of unusual organ involvement.
5. High mortality rate despite optimal therapy.

Classification criteria for CAPS-

a) Evidence of involvement of 3 or more organs,systems and/or tissues.
b) Development of manifestations simultsneously in/or less than a week.
c) Confirmation by histopathology of small vessel occlusion.
d) Lab confirmation of the presence of anti-phospholipids antibodies.

Definite CAPS – all 4 criteria present.

Probable CAPS –

- all 4 criteria except only 2 organs, systems, and/or tissues involved.
- All 4 criteria , except for the absence of lab confirmation of antiphospolipid antibodies.
- Criteria a,b and d.
- Criteria a,c ,d with development of a third event more than 1 week but within 1 month of presentation , despite anticoagulation.

We present this case to draw attention to this little-knowninfection, rat bite fever with a rare complication of native valve endocarditis with secondary APLA syndrome. This case report also highlights the importance of a good history, the utility of good culture techniques and transesophageal echocardiography in diagnosis and ensuring the completion of the course of antibiotics.

IV. CONCLUSION

Clinicians should consider rat bite fever in the differential diagnosis of an unexplained febrile illness, especially in patients with relapsing or intermittent fever. **Enquiring into history of bites is important when evaluating a pyrexia of unknown origin(PUO) as patients may forget it or dismiss it as inconsequential. Native valve endocarditis on a structurally normal valve is extremely rare and requires blood culture or polymerase chain reaction(PCR) and echo for diagnosis**. Transesophageal echocardiographis preferred whenever there is a bacteremia, no obvious focus and suboptimal transthoracic imaging. Adequate antibiotic therapy (dose and duration) is also important in preventing complications and completely eradicating the infection.In conclusion, RBF should be considered and evaluated for in the workup or cases of culture negative infectious endocarditis in patient with compatible clinical presentations, particularly if they report any rodent exposure.

CAPS patient suffer from a life threatening acute multiple organ thrombosis, usually accompanied by microthrombosis and hematological manifestations with high titre of antiphospholipid antibodies. In our patient the occurrence of so many manifestations simultaneously over a short span confirmed the diagnosis of catastrophic APLA syndrome. Without early diagnosis and treatment, prognosis is poor. It is important to anticipate CAPS and CAPS like disease in young patients with multiorgan involvement and overlapping other thrombotic microangiopathies and known triggering factors in order to halt the mortality and improve prognosis.

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