Necrotizing fasciitis with group A Streptococci and Eggerthella lenta as a complication of Varicella in a child

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ABSTRACT
Necrotizing fasciitis is a life threatening condition that can be quickly spread through the flesh surrounding the muscle. The disease can be polymicrobial, or caused by group A beta hemolytic Streptococci, or by Clostridium spp. We present a case of a 7 years old girl, which was hospitalized in Children Infectious Diseases Department in a 7th day of chickenpox (hematic crusts all over the body), high fever, asthenia, vomiting, oligoanuria, and tumefaction, pain and functio lessa in the right thigh. In a very short time in the right thigh swelling, edema and congestion have increased gradually, and in the third highest middle thigh the ecchymotic areas appeared evolving towards bubbles and blisters which included the right thigh and calf. After excluding the diagnosis of thrombophlebitis was raised suspicion of necrotizing fasciitis. CT pelvic scan evidenced pelvic asymmetry by maximus and medium right gluteal muscles swelling with important inflammatory infiltrate extended laterally in the subcutaneous adipose tissue. In blood culture was isolated Eggerthella lenta, and from throat swab was isolated group A Streptococci. Treatment consists of a combination of antibiotics associated with intravenous immunoglobulin administration. Despite medical treatment evolution worsened and required transfer in a pediatric surgery department where emergent surgical debridement associated with intensive antibiotic therapy was done. After this intervention evolution was slowly favorable without major limb dysfunction. Polymicrobial necrotizing fasciitis is a severe disease, which if recognized early can have a favorable outcome.

Keywords: Streptococci group A, Eggerthella lenta, necrotizing fasciitis, varicella, child

Introduction
Necrotizing fasciitis (NF) is a life threatening condition as consequence of bacterial infection of the soft tissue that can be quickly spread and destroys the subcutaneous fat and fascia which surrounding the muscle [1,2,3,4]. However the general symptoms like common cold are present and local signs of infection, such as inflammation and redness of infected limb, or blisters with clear fluid, and sometimes even a minor skin lesion near the affected area. Severe pain is almost always present in affected area, with discordance between intensity of the pain and rash size or skin lesion. [3,5]. In early stage of NF cellulitis is easily
mistaken. The most important factor that differentiates these two conditions is the fact that cellulitis responds to antibiotics whereas necrotizing fasciitis does not [3]. There are many risk factors that contribute to NF, from which the most common were: intravenous drug use, immune-deficiencies, chronic diseases such as diabetes or chronic heart/pulmonary diseases, skin injury, and varicella [2]. In the last years many studies suggest that in patients treated with non-steroidal anti-inflammatory drugs increased the risk of NF [6,7,8].

In literature there are described three types of NF [2]:
- type I in which more than one bacteria is involved; most common bacteria involved in this type were: Staphylococcus aureus, Haemophilus, and some other aerobic and anaerobic germs;
- type II which is caused by group A Streptococci (GAS);
- type III in which the most common germs involved were Clostridium perfringens or Clostridium septicum [2];

Type I and type III generally follows significant injury or surgery, and type II is common in children with chickenpox [2].

The illnesses caused by GAS have been divided into two categories:
- the less serious and noninvasive infections;
- the more serious and invasive infections;

The noninvasive GAS infections include tonsillitis, scarlet fever, impetigo, and rheumatic fever. Invasive diseases caused by GAS were necrotizing fasciitis and streptococcal toxic shock syndrome which can cause rapid death. Cases of NF caused by GAS untreated or with delayed treatment can turn into streptococcal toxic shock syndrome [3,9,10].

Although aggressive surgery is important for survival, we do not know exactly the impact of various germs involved in the favorable evolution of patients [1,2,3]. In cases of necrotizing fasciitis antibiotics administration in combination with surgery (immediate debridement of necrotic tissue) is usually the best treatment [11].

Case presentation

We present a case of a 7 years old girl, which was hospitalized in Children Infectious Diseases Department in a 7th day of chickenpox (hematitic crusts all over the body), high fever, asthenia, vomiting, and oligo-anuria. She was hospitalized in our department just for 3 days. Since the beginning of hospitalization she presented in the right thigh tumefaction, pain and functio lessa. In a very short time in the right thigh swelling, edema and congestion have increased gradually, and in the third highest middle thigh the ecchymotic areas appeared and evolving towards bubbles and blisters which included the right thigh as we can see in figure no. 1; and calf in the last day of hospitalization in our department..

Figure 1 - Right thigh swelling with ecchymotic areas and blisters

In the first 24 hours of hospitalization a CT scan performed evidenced pelvic asymmetry by maximus and medium right gluteal muscles swelling with important inflammatory infiltrate extended laterally in the subcutaneous adipose tissue, cranial on posterior contour lines of right paravertebral muscles and caudal along the internal face of the fascia lata and posterior from the square neck on the maximus gluteal deep contour to its femoral insertion. Diffuse inflammatory infiltration of the sub-peritoneal fat, obvious to the right, including the mesorectal tissue, with mass effect on pelvic structures which are diverted to the left (as we can see in figure 2).
After excluding the diagnosis of cellulitis and thrombophlebitis of right inferior limb was raised suspicion of necrotizing fasciitis. Cellulitis was excluded by no response to antibiotics and thrombophlebitis by Doppler ultrasound.

Over the short period of hospitalization in our department evolution of biological markers was unfavorable and is presented in table no. 1. We noticed an important increased in white blood counts with increased neutrophils, and increased levels of inflammatory test: erythrocyte rate sedimentation (ESR) fibrinogen and C reactive protein (CRP).

Polymicrobial etiology was established as consequence of isolation of two germs in blood culture and in throat swab. Eggerthella lenta a gram positive bacillus was isolated from anaerobe blood culture. Presence of group A beta hemolytic Streptococci was certified by increased antistreptolysine O titer (ASLO) and isolation of bacteria from throat.

Treatment consists of a combination of antibiotics associated with intravenous immunoglobulin administration. Antibiotic association used in this case was: Metronidazol + Meropenem and because Staphylococcal etiology was still in discussion we add Linezolid in the second day of hospitalization. In first 48 hours of hospitalization we used this broad spectrum association of antibiotics because gram positive and negative germs were taken into consideration as well as anaerobic germs. Because it was considered a serious condition since the beginning, in the context of chickenpox, we administered intravenous immunoglobulin.

Table 1 - Blood test over period of hospitalization

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1st day</th>
<th>2nd day</th>
<th>3rd day</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood count (Normal value: 4-12x10³ cells/mmc)</td>
<td>12800</td>
<td>20900</td>
<td></td>
</tr>
<tr>
<td>Lymphocyte (Normal value: 25-55%)</td>
<td>6.1%</td>
<td>6.9</td>
<td></td>
</tr>
<tr>
<td>Neutrophils (Normal value: 35-65%)</td>
<td>84.6%</td>
<td>82.1</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin level (Normal value: 12-15.5 g/dl)</td>
<td>13.5</td>
<td>9.5</td>
<td></td>
</tr>
<tr>
<td>Platelets (Normal value: 150 – 350 x 10³ /µL)</td>
<td>193000</td>
<td>158000</td>
<td></td>
</tr>
<tr>
<td>Erythrocyte rate sedimentation (ERS) (Normal value: 3-9 mm/1h)</td>
<td>20</td>
<td>40</td>
<td>65</td>
</tr>
<tr>
<td>Fibrinogen (Normal value: 150-350 mg%)</td>
<td>580</td>
<td>880</td>
<td></td>
</tr>
<tr>
<td>C reactive protein (CRP) (Normal value: &lt;6 mg/L)</td>
<td>&lt;6</td>
<td>12</td>
<td>48</td>
</tr>
<tr>
<td>ALT (Normal value: 0-42 U/L)</td>
<td>27</td>
<td></td>
<td>45</td>
</tr>
<tr>
<td>AST (Normal value: 0-37 U/L)</td>
<td>62</td>
<td></td>
<td>146.5</td>
</tr>
<tr>
<td>Urea (Normal value: 10-45 mg/dl)</td>
<td>65</td>
<td>97.8</td>
<td>96</td>
</tr>
<tr>
<td>Creatinine (Normal value: 1-1.2 mg/dl)</td>
<td>1.66</td>
<td>1.78</td>
<td>1.05</td>
</tr>
<tr>
<td>ASLO titer (antistreptolysine O titer) (Normal value: &lt; 200 U)</td>
<td>1200</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swab from throat</td>
<td>Group A Streptococci</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood culture</td>
<td>Eggerthella lenta</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV1+2 antibody (Normal value: negative)</td>
<td>Negative</td>
<td></td>
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</table>
Despite medical treatment evolution worsened in hours in the last day of hospitalization in our department and required transfer in a pediatric surgery department where emergent surgical debridement associated with intensive antibiotic therapy was done. The antibiotic treatment used after results from blood cultures was an association of Penicillin G with Metronidazole. After this intervention evolution was slowly favorable without major limb dysfunction, but after one month plastic surgery was necessary.

**Discussions**

NF is a severe but rare bacterial complication, caused by GAS in children with varicella. There were many studies published all over the world which describes this rare but potentially lethal complication in children with chickenpox [1,6,8,11,12]. In our case in addition of GAS we noticed also presence of Eggerthella lenta which may cause life-threatening disseminated infections with initial source from various site including soft tissue (like in our case) [13,14]. Association of these two germs, which may have each separate, aggressive life-threatening evolution, can explain the rapid evolution of the disease in this case.

Invasive streptococcal complications in varicella were evidenced by a retrospective study done by Aebi C et al., in 84 patients younger than 16 years of age, over a period of 10 years. In this study from total streptococcal complications almost half of them were invasive infections [12].

In a study performed by Hsiao CT et al., about predictors factor of mortality in NF they found that Aeromonas infection, Vibrio infection, cancer, hypotension, and band form white blood cell count greater than 10% are positive predictors of mortality; while Streptococcal and staphylococcal infections, are not predictors of mortality. In the same study they found that the presence of hemorrhagic bullae is a negative predictor of mortality [1].

In another study performed by Lesko SM et al. about 52 cases of invasive GAS infection, including 21 with NF they found that, risk of invasive GAS infection was increased among children who were nonwhite, living in low-income households, exposed to varicella at home, or had a persistent high fever. In studies of Lesko SM et al. and Souyri C et al. they noticed that use of nonsteroidal anti-inflammatory drugs increase the risk of invasive GAS infection including necrotizing complications in all patients, because their use delay diagnosis by hiding the symptoms [5,7]. Like in these studies in our case we increased the risk of invasive GAS by using during first days of hospitalisation anti-inflammatory treatment with Ibuprofen.

The conclusions of study performed by Clark P et al., about NF secondary to chickenpox infection in children was that this condition should be suspected in any child with a history of varicella infection and complaint of pain and swelling in a different body area associated with increasing fever, erythema, lethargy and irritability [11]. According with this study in our case were present all these serious and suggestive signs for NF which widened gradually, and led to a rapid setting of the diagnosis in the first 48 hours.

Given the severe and fulminant evolution of the case has been taken into discussion a major cause of immunosuppression, which was excluded by negative HIV test.

**Conclusions**

Necrotizing fasciitis is a severe disease, which if it’s recognized early can have a favorable outcome. In cases in which were associated two germs like group A beta hemolytic Streptococci and Eggerthella lenta the diseases evolution could be more rapid and aggressive.

In cases of NF besides intensive antibiotic therapy is essential a rapid surgery with debridement and drainage in order to prevent muscle necrosis major limb dysfunction and death.
References