Purpura fulminans: A rare condition that surprisingly develops after endoscopic retrograde cholangiopancreatography

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Abstract
Purpura Fulminans (PF) is a disease that occurs after septicemia. It has a rapid course. PF causes disseminated intravascular coagulation and severe organ failure. Extremity amputation and fatality rates are very high, even if it is diagnosed and treated promptly. This case report presented a 59-year-old man who developed purpura fulminans after Endoscopic Retrograde Cholangiopancreatography (ERCP).

Introduction
Purpura Fulminans (PF) is a rare disease with microvascular thrombosis and dermal hemorrhages affecting all age groups. High fever, tachycardia, and hypotension are the most common findings, and it progresses to peripheral circulatory collapse and shock in a short time. The mortality rate is very high. It often occurs during infection or within 2-4 week. PF is seen generally after Meningocemia, infection with Haemophilus spp., and diseases such as chickenpox [1]. The lesions are sharply circumscribed, symmetrical and usually peripherally located. These lesions often turn into gangrene and require amputation. Sometimes, amputation can be prevented by extensive debridement and grafting [2].

Up to our knowledge this is the first article describing after Endoscopic Retrograde Cholangiopancreatography (ERCP). However, there are eight articles on the development of purpura fulminans due to E. coli. Most of these have been seen in the neonatal and childhood period. Two of them were seen in adulthood [3-8]. A specific strain of E. coli (Group A E. coli) was found in one case report. Most PF cases developed after urinary tract infections and one case report was seen after heart transplantation [9]. We presented a case of fatal outcome due to PF after ERCP.

Case
ERCP was performed and a plastic stent had been placed for a 59-year-old male patient due to choledocholithiasis. The patient went to the same center for stent removal one year after the first procedure. The plastic stent was found migrated into the common bile duct. It could not be removed despite significant efforts, and he was referred to our center. The patient did not have any complaints at admission, and his physical examination and blood tests were within normal limits. His past history was, otherwise, negative. The migrated stent was removed with spyglass cholangioscope. He was well in the next morning, blood tests were normal and oral intake was started. The patient complained of sweating in the twentieth hour after the procedure, but no fever or hemodynamic changes were detected. However, it was observed that the previously normal CRP increased to 71 mg/L (reference range 0-5 mg/dl), and the procalcitonin level, which was not measured before, was 48 mg/L (baseline value <0.5 mg/L). A blood sample was taken for culture. Parenteral fluid and intravenous antibiotics ceftriaxone...
Intravascular Coagulation (DIC). Although PF is mainly seen in
therapy with protein C concentrates and Fresh Frozen Plasma (FFP),
thrombotic thrombocytopenic purpura were not considered.
any schistocyte or atypical cells. Hemolytic uremic syndrome
with hematology. His peripheral blood smear did not reveal
due to poor general condition. The patient was also consulted
recommended antibiotic therapy, keeping the limbs warm and
encouraged. In case of necrosis, wet dressing due to the development of granulation tissue in
prolongation of peripheral arterial filling time was detected. He was
taken to the intensive care unit to continue his treatment the
first forty-eight hours after the procedure, positive intravenous treatment was started
intravenously. Forty-eight hours after the procedure, rapid progresssion of ecchymosis on the fingertips, penis head,
ear side, and nose was observed, and loss of consciousness de-
veloped. No pathology was detected to explain the situation on
the computed tomography of the brain. Heparin infusion was
started. White blood cell count was 54000 /µL (reference range
4000-10000 /µL), hemoglobin level was 9.96 g/dl (ref. ran.: 12-14 g/dl), platelet count was 57000 /µL (ref. ran.: 150000-
450000 /µL) at the laboratory test. Vasculitic blood tests and
coagulation parameters were analyzed due to the differential
diagnosis of a rapidly progressive vasculitic picture, DIC (dis-
seminated intravascular coagulation), sepsis, and TTP (throm-
botic thrombocytopenic purpura). ANA, anti-ds DNA, protein C,
protein S, antidiolipin antibodies, anti-beta 2 glycoproteins
1 IgG, IgM, p-ANCA, and lupus anticoagulants were negative.
Anti-thrombin 3 antigen was low, and antithrombin-3 activity
was low. Escherichia coli growth in two blood cultures and
only Acinetobacter baumani growth (sensitive to colistin) was
detected in the tracheal aspirate. Colistin, meropenem, and
evancocyn treatment were started. ERCP was performed two
more times on the second and third days of his intensive care
stay. Pus drainage was observed after biliary cannulation. The
area was washed with antibiotics, and nasobiliary drainage was
taken. On the fourth day of the intensive care follow-up, the
patient was taken to Continuous Renal Replacement Therapy
(CRRT) in the intensive care unit due to an anuric state. The
ecchymotic areas of the patient turned into gangrene. Skin-punch
biopsy revealed orthohyperkeratosis on the surface. Nearly
complete necrosis in the epidermis, ischemic changes, and
thrombosed vascular structures was seen in the upper dermis.
Erythrocyte extravasation and solar degeneration were found.
All these findings supported purpura fulminans. Plastic surgery
consultation was requested when the demarcation line became
evident in the ecchymosis areas of the patient. Plastic surgery
recommended antibiotic therapy, keeping the limbs warm and
wet dressing due to the development of granulation tissue in
the demarcation line. They did not recommend escharotomy
due to poor general condition. The patient was also consulted
with hematology. His peripheral blood smear did not reveal
any schistocyte or atypical cells. Hemolytic uremic syndrome
or thrombotic thrombocytopenic purpura were not considered.
The patient died on the 12th day of hospitalization despite the
maximum antibiotic therapy, immunosuppressive therapy, ther-
apy with protein C concentrates and Fresh Frozen Plasma (FFP),
and inotropic support.

Discussion

Purpura Fulminans (PF) is a thrombotic type of Disseminated Intravascular Coagulation (DIC). Although PF is mainly seen in
newborns, it may rarely be seen in adults as well. In most of the instances, it develops after an infection, mostly bacterial (either
gram negative or positive), sometimes viral. Meningococcus is
the most common cause of PF and its mortality rate is 15-25%.
Haemophilus influenza, Capnocytophaga canimorsus, strepto-
coccus species, and staphylococcus aureus species have also
been shown as other infectious causes of PF (Table 1). Dysfunction
of endogenous anticoagulant pathways after infection is re-
sponsible for its pathophysiology. Inherited protein C (PC) and
S (PS) deficiency have been associated with PF. PROC and PROS
1 genes were identified as responsible genes for PF as well. Decreased protein C, protein S, and antithrombin III levels due to
cytokines activated by bacterial Autoantibodies against proteins
C and S have been detected in patients with PF 7-10 days after
infection. It has been observed that cross-reacting IgG-type an-
tibodies increase the clearance of protein S. Protein C is a serine
protease; it has anti-inflammatory and cytoprotective effects.
Loss of endothelial thrombomodulin and decreased efficacy of
activated protein C have been demonstrated in PF patients [10].
In a study by Lerolle et al., they compared the patients with Pur-
pura fulminans and sepsis and those with sepsis and DIC. In the
prevalence of PF, bacteria in the vascular bed, bacterial endotox-
in, changes in endothelial protein C receptor, change in CD 31
marker, and change in thrombomodulin were detected. Most
PF patients are found to be positive for lupus anticoagulants.
Asplenism, immunosuppressive diseases, heterozygous factor V
Leiden mutation, alcohol use, and abnormal complement levels
are other risk factors associated with PF [11].

In the early clinical presentation of PF patients, livedo reticu-
laris appears on the extremities, ear, nose tips, back, and hips,
following the latent period after infection. Afterward, areas of
dermal vascular thrombosis and necrosis appear in the middle of
these areas. If bleeding occurs in the necrosis areas, hemor-
rhagic bullae appear. Within 24-48 hours, full-thickness necrosis of
dermis settles. This feature differs from other diseases, such as ITP and TTP. The skin biopsy specimen can show thrombi
within the dermal vascular structures histologically. End-organ
damage is caused by vascular thrombosis. Later, hard eschars
are formed. Bilateral, symmetrical involvement of the extremi-
ties is a typical finding. It is known that there is a very close
relationship between the severity of skin lesions and protein C
levels. Therefore, protein C concentrate or FFP should be start-
ed on patients without delay. Intravenous heparinization and,
if necessary, antithrombin III can be used. Anti-coagulation and
factor replacement therapies are at the most effective to pre-
vent thrombosis-related end-organ damage. Thrombotic com-
plications can occur long after the infection resolved. Mortality is
very high. Most survivors have an amputation of the affected
area [10-13].

In our case, the lesions were bilateral and symmetrical, with
clear borders (Figures 1,2). The transformation of the post-
infection lesions from livedo reticularis to necrosis developed
within hours. Despite the administration of anticoagulants, anti-
 thrombotic therapy, protein C concentrate, and FFP in the early
phase, necrosis and end-organ damage could not be prevented.
Escharotomy, wound debridement, allografting, xenografting,
or synthetic dressings can be used when the boundaries of
necrosis become clear. It prevents fluid, electrolyte, protein loss,
secondary bacterial infection, and increased catabolism can be

Citation: Tosun SD, Koçhan K, Kiremitçi S, Köker IH, Şentürk H. Purpura Fulminans: A Rare Condition that Surprisingly Devel-
prevented [10]. In our case, we tried to prevent this by us in wet dressing and keeping warm.

Warfarin-induced skin necroses, cryoglobulinemia, Anti-Phospholipid Syndrome (AFLS), Heparin-Induced Thrombocytopenia (HIT), and Henoch-Schonlein Purpura (HSP) should be considered in the differential diagnosis. All were discard in our case.

Although E. coli is not frequently cited as the cause of PF, intestinal and extraintestinal E. coli related case with specific strain have been reported. In our case, Escherichia coli growth was detected in two sets of blood cultures. Broad-spectrum antibiotics were started. Two more biliary cannulations were performed after the first ERCP to ensure infection control, and pus drainage was provided. Although infection control was achieved, end-organ damage developed due to thrombotic complications, and the patient died.

Table 1: Reasons for Purpura Fulminans.

<table>
<thead>
<tr>
<th>Genetic factors</th>
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<tbody>
<tr>
<td>- Protein C deficiency</td>
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<tr>
<td>- Protein S deficiency</td>
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<tr>
<td>- Factor V Leiden mutation</td>
</tr>
<tr>
<td>- Abnormal complement level</td>
</tr>
<tr>
<td>Infectious diseases</td>
</tr>
<tr>
<td>- Meningococ infection</td>
</tr>
<tr>
<td>- Pneumococ infection</td>
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<tr>
<td>- Haemophilus infection</td>
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<tr>
<td>- Streptococcus species</td>
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<tr>
<td>- Varicella infection</td>
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<tr>
<td>- Capnocytophaga canimensuris infection</td>
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<td>- Staphylococcus aureus infection</td>
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<tr>
<td>Autoimmune diseases</td>
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<tr>
<td>- Autoimmune protein C and S deficiency</td>
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<tr>
<td>Cholestatic diseases</td>
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<td>- Cholangitis</td>
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<td>- Gall Blader infection</td>
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<td>Drugs</td>
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<td>- Warfarin</td>
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<td>Immune compromised diseases</td>
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<tr>
<td>- HIV</td>
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<tr>
<td>- Splenectomy before</td>
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<td>- Acquired abnormal complement level</td>
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Figure 1: The lesions were bilateral and symmetrical, with clear borders.

Figure 2: Gangrene at the fingertips and hands.

Although early diagnosis and treatment reduces mortality, significant morbidity results. In summary, we described a patient developed Purpura fulminans after ERCP due to E. coli cholangitis who was lost despite timely exertion of all available management methods.

Conclusion

Purpura fulminans is an acute, thrombotic, devastating emergency with high mortality. We are yet to know what exactly triggers purpura fulminans. It has been observed that some risk factors mentioned above lay the ground for this condition.

References

3. Lowry J, Noel E. A Rare Cause of a Rare Disorder: E. coli-Induced Purpura Fulminans Secondary to Urinary Tract Infection. Case Reports in Critical Care. 2022.