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Necrotising fasciitis in a patient with monoclonal gammopathy of undetermined significance

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Lesson

To consider the potential risk of an unprovoked infectious disease, such as necrotising fasciitis, being present in patients whereby monoclonal gammopathy of undetermined significance is an active co-morbidity.

Keywords
clinical, infectious diseases, trauma and orthopaedic surgery

Abbreviations

IgG: Immunoglobulin G, **IgA:** Immunoglobulin A, **IgM:** Immunoglobulin M, **IgE:** Immunoglobulin E, **NaCl:** Sodium Chloride, **Na^+:** Sodium, **K^+:** Potassium, **O_2:** Oxygen, **pO_2:** Partial pressure of oxygen, **pCO_2:** Partial pressure of carbon dioxide, **HCO_3:** Bicarbonate.

Case report

A 52-year-old man was admitted to accident and emergency following a three-day history of a painful, oedematous right hand associated with an erythematous rash which had previously been treated by his doctor with flucloxacillin for three days. On admission, the rash had worsened and covered his entire face and the proximal third of his torso but there was no evidence of regional skin hypoaesthesia, crepitus, development of haemorrhagic blisters or any gangrenous changes. The patient had a history of asthma, for which he was receiving daily steroids, bronchiectasis, chronic kidney disease (stage III), hypertension, alcoholic liver disease and monoclonal gammopathy of undetermined significance.

Pre-admission serum immunoglobulin levels were all elevated as follows: IgG: 16.9 g/L; IgA: 4.64 g/L; IgM: 1.09 g/L; IgE: > 5000 g/L. His baseline serum immunoglobulin levels taken in March 2016 show chronic elevation, with levels higher than that of this admission: IgG: 18.6 g/L; IgA: 4.72 g/L; IgM: 0.97 g/L; IgE: > 5000 g/L.

Upon admission, the precise nature of the rash was still unclear and an allergy to flucloxacillin was not fully excluded as a contributing factor.

His observations on admission were as follows: O_2 saturations: 98% on air; respiratory rate: 19; blood pressure: 101/49; heart rate: 108; capillary refill time: 4 seconds; temperature: 35.4°C; the patient's Glasgow coma scale was 15/15, he was alert and orientated.

Subsequently, the flucloxacillin was halted in case this was an anaphylactic reaction and the sepsis 6 protocol was initiated with intravenous teicoplanin, ertepenem, clindamycin, warmed 0.9% NaCL along with intramuscular adrenaline, intravenous hydrocortisone and intramuscular chlorphenamine.

Laboratory studies showed:

White blood cells: 10.9×10^9/L; haemoglobin: 136 g/L; platelets: 98×10^9/L; neutrophils: 9.6×10^9/L; C-reactive protein: 415 mg/L; urea: 15.3 mmol/L; creatinine: 284 µmol/L; Na +: 128 mmol/L; K +: 5.9 mmol/L; estimated glomerular filtration rate: 20 ml/mm/1.73 m^2; bilirubin: 33 µmol/L; alanine transaminase: 25 U/L; alkaline phosphatase: 60 U/L; albumin: 28 U/L; gamma gutamyltransferase: 139 U/L; albumin: 28 g/L; prothrombin time: 13.4 seconds.

Within hours of admission, the skin rash had alarmingly spread down the patient's back and now involved his buttocks. The patient was still alert but his O_2 saturations had dropped to 90% on 15 L of oxygen and so an arterial blood gas was obtained:

pH: 7.15; pO_2: 7.85 kPa; pCO_2: 6.54 kPa; HCO_3: 16.7 mEg/L; Na+: 127.4 mmol/L; K+: 5.13 mmol/L; lactate: 6.4 mmol/L; base excess: 12.1 mmol/L; glucose: 11.4 mmol/L.

A laboratory risk indicator for necrotising fasciitis (LRINEC) score was calculated as 9 for this patient's condition meaning that there was an elevated probability that the team were dealing with a case of necrotising fasciitis. A score of 9 suggests a higher mortality rate and a significantly increased amputation risk.[1,2]

Subsequently a computed tomography scan was performed which confirmed appearances consistent with necrotising fasciitis involving the whole of the superficial fascia of the upper arm. He was taken to theatre for debridement of all the necrotic/infected

Figure 1. Coronal view of computed tomography neck/ chest/ abdomen/ pelvis showing widespread subcutaneous right arm oedema extending into the axilla.

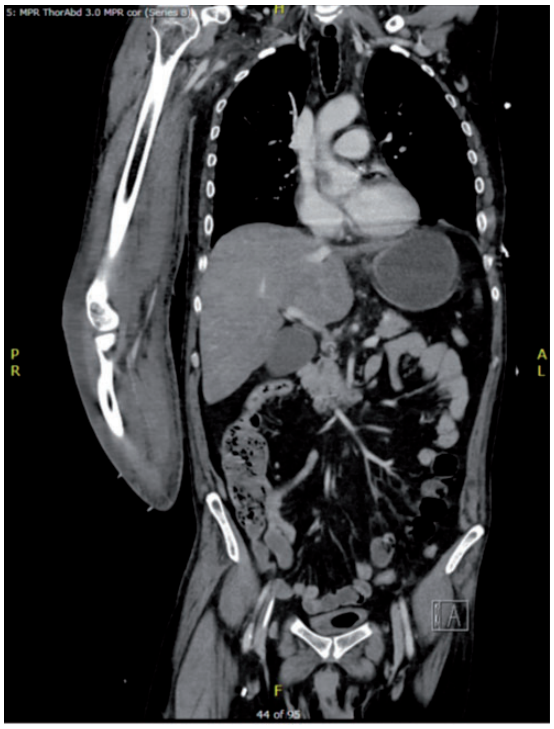
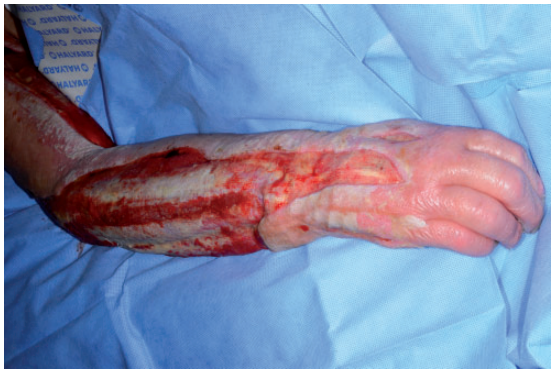


Figure 2. Right upper limb following initial surgical debridement.



tissue. Tissue culture from theatre yielded *Group A beta haemolytic streptococcus*. Following three more debridements and a prolonged stay in intensive treatment unit with inotropic support he recovered sufficiently to allow the plastic surgery team to begin skin grafting of the debrided areas.

Discussion

The incidence of necrotising fasciitis has increased in recent decades in several different countries. Arguably, the most concerning aspect of this is the high mortality rate that is associated with necrotising fasciitis, and this underlines the importance of identifying high-risk patients and considering the diagnosis of necrotising fasciitis early.

Necrotising fasciitis may result from any major or minor injury to the skin such as needle puncture, insect bites, burns, lacerations, surgical wounds or blunt trauma that can act as an entry point for the causative organism. However, an entry point for bacteria cannot always be determined and this is also the case for our patient.

Common co-morbidities predisposing to necrotising fasciitis are diabetes mellitus, malignancies and connective tissue disorders such as rheumatoid arthritis/systemic lupus erythematosus. These conditions are treated with rheumatological immunosuppressive medications and glucocorticosteroids. The patient in this case report was taking 10 mg of prednisolone daily for asthma for several years. The association of steroid treatment with necrotising fasciitis has been reported previously.[3] Angoules et al. analysed the literature on necrotising fasciitis between 1992 and 2007 and they concluded that 3% of the documented necrotising fasciitis cases were associated with corticosteroid therapy. On the contrary, there is no direct mention of an association between asthma and necrotising fasciitis.[4]

After analysing 131 papers, Angoules et al. found examples in the literature indicating that chronic kidney disease was related with 3% of necrotising fasciitis cases,[4] mirroring the risk caused by corticosteroids. There are other examples of case reports that indicate that there is a link between chronic kidney disease and necrotising fasciitis; however, they are usually associated with either renal transplants or haemodialysis.[5,6] Despite the patient having no history of renal transplant or haemodialysis for his stage III chronic kidney disease, immunosuppression should not be overlooked as a possible predisposing factor as there are plenty of examples in the literature suggesting that chronic kidney disease itself is associated with immunosuppression.[6]

Angoules et al. further speculated that alcoholic liver disease was a significant predisposing factor present in 17% of the cases in his review.[4]

The final co-morbidity that should be considered is monoclonal gammopathy of undetermined significance, a premalignant disorder involving abnormal proliferation of monoclonal plasma cells in the bone marrow. Patients with monoclonal gammopathy of undetermined significance have a lifelong risk of

multiple myeloma which is associated with a median survival of 4–5 years. In 2012, Kristinsson et al. reported on a monoclonal gammopathy of undetermined significance cohort from a national hospital network in Sweden between 1965 and 2005 that compared 5326 monoclonal gammopathy of undetermined significance patients and 20,161 population matched controls. Patients with monoclonal gammopathy of undetermined significance in his study had a 2.1-fold (95% confidence interval: 2.0–2.3) increased risk of developing bacterial infections (osteomyelitis, septicaemia, pyelonephritis, cellulitis, endocarditis and meningitis) and viral infections (influenza and herpes zoster) ($p < 0.05$). At 5- to 10-year follow-up, 377 monoclonal gammopathy of undetermined significance patients (7.1%) were found to have more than one infection compared to 550 control patients (2.3%) during the same period of time.[7] An earlier and smaller study was conducted in Denmark by Gregersen et al. which similarly found that patients with monoclonal gammopathy of undetermined significance have a two-fold increased risk of suffering with bacterial infections.[8]

The predisposition to infection in monoclonal gammopathy of undetermined significance patients may be associated with a defective polyclonal immunoglobulin antibody response. Similar defects are observed in patients with multiple myeloma and Waldenström macroglobulinemia.[9,10] There are numerous reports of patients with multiple myeloma developing infections including necrotising fasciitis[11] but a direct connection with monoclonal gammopathy of undetermined significance has not been reported despite there being examples of patients in case reports suffering with monoclonal gammopathy of undetermined significance and contracting necrotising fasciitis.[12]

Conclusions

Our case raises the possibility that monoclonal gammopathy of undetermined significance, which is considered a precursor of multiple myeloma, can also lead to necrotising fasciitis, although because of the simultaneous presence of additional predisposing factors, a definitive connection cannot be made based on our case alone.

Declarations

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Guarantor: JXV

Contributorship: JXV: Conception, research and design of the case report; obtaining informed consent from patient; first draft of case report; revision and subsequent final approval of the version to be submitted. RPJ: Guidance throughout and subsequent final approval of the version to be submitted.

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