

Case report

Efficacy of colistimethate sodium as local application in necrotising fasciitis

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Accepted 9 November 2019

SUMMARY

Necrotising fasciitis (NF) is a rapidly progressive severe soft tissue infection of the deep fascia resulting in the destruction of overlying subcutaneous tissue and skin. We report the case of NF of the lower limb with a poor prognosis due to multidrug-resistant (MDR) *Klebsiella pneumoniae* (*K. pneumoniae*) sensitive only to colistin. In view of the worsening condition of the wound, risk of deterioration of renal function and economic constraints, it was decided to start on colistin therapy locally by colistimethate sodium (CMS). The patient responded well to the treatment and got clinically better. Subsequent culture sent for post-treatment showed no growth of the organism. The wound healed with regular dressings by 8 weeks. This was found to be a very cost-effective treatment modality. Local use of CMS was found to be a novel method of achieving infection-free wound especially against MDR *K. pneumoniae*.

BACKGROUND

Necrotising fasciitis (NF) is common in the surgical ward and is difficult to treat. Sepsis is very common in these patients and if they present to the hospital late, mortality is very high.¹ In an economically compromised patient, cost of higher antibiotics makes optimum treatment impossible. Here, we present a patient who had an infected wound with an aggravated systemic response. Culture revealed *Klebsiella pneumoniae* (*K. pneumoniae*) sensitive only to colistin. Parenteral colistin is expensive and this patient also had a risk of progressively worsening renal parameters, which rendered colistin dangerous to administer. In a cash-strapped nation like ours, a novel method of using colistin locally in the wound gave us excellent results without compromising the patient's health or finance.

CASE PRESENTATION

Our patient was a 29-year-old man on therapy for chronic myeloid Leukaemia (CML), referred to us with deep vein thrombosis (DVT) and compartment syndrome right thigh. CML was in the chronic phase but since he had a severe infection, his total count was 656.0 K/ μ L, 4% blast cells on peripheral smear. On examination, his right thigh was swollen, tender and red. There were blisters in the right thigh with features of early compartment syndrome. The patient was diagnosed to have NF with compartment syndrome and fasciotomy with wound debridement was done. The subcutaneous tissue, fascia and muscles in the adductor and anterior compartment

of the thigh were necrotic (figure 1) and there were pus pockets around the femoral vessels extending cranially into the iliac area and the caudal extent was till the lower-third of the thigh. Culture from the wound showed heavy growth of multidrug-resistant (MDR) *K. pneumoniae* (figure 2) sensitive only to colistin. Blood culture showed no growth. The patient had a severe local infection with a systemic response, serum creatinine was 1.17 mg/dL and intravenous colistin being nephrotoxic was not advisable for systemic therapy. Each vial of colistimethate sodium (CMS) (4.5 million IU) (Xylistin, Cipla) cost 3500 INR (Indian rupees). An 8 hourly regimen for 5–7 days would cost about 70 000 INR. Diabetic wound infections have been treated successfully using carriers for local delivery of antimicrobial agents.² In view of high cost and fear of renal function deterioration due to sepsis and drug side effect, we tried a similar but cost-effective method of colistin therapy locally. One vial of CMS was mixed with a tube of debridace (15 g) ointment containing (pappain 521 700 IU+urea 100 mg) (Virchow Healthcare). Half of the mixture was applied over the wound per day after debridement and the remaining mixture was refrigerated and used the next day. We applied this mixture on the wound for 2 weeks working out to about 15 000 INR for the patient. Patient responded well to the treatment (figure 2). His serum creatinine after 2 weeks was 0.79 mg/dL. Subsequent culture sent for post-treatment showed no growth of the organism. This was found to be a very cost-effective treatment modality.

INVESTIGATIONS

- ▶ Culture from the wound showed growth of MDR *K. pneumoniae* sensitive only to colistin.
- ▶ Preoperative creatinine—1.17 mg/dL.
- ▶ Creatinine after 2 weeks—0.79 mg/dL.
- ▶ Total count 656.0 K/ μ L.
- ▶ Peripheral smear—normocytic, normochromic red blood cells (RBCs), polychromatophils+, 6nRBC/100 white blood cell (WBCs), few ovalocytes, blasts cells –4%, band and metamyelocytes 32%, myelocytes and promyelocytes 23%, and platelet count $3.34 \times 10^9/L$.

TREATMENT

Each vial of CMS (4.5 million IU)(Xylistin, Cipla) cost 3500 INR. An 8 hourly regimen for 5–7 days would cost about 70 000 INR. Diabetic wound infections have been treated successfully using



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To cite: Murali S, Pillai AV, Ramachandran R. *BMJ Case Rep* 2019;**12**:e232354. doi:10.1136/bcr-2019-232354

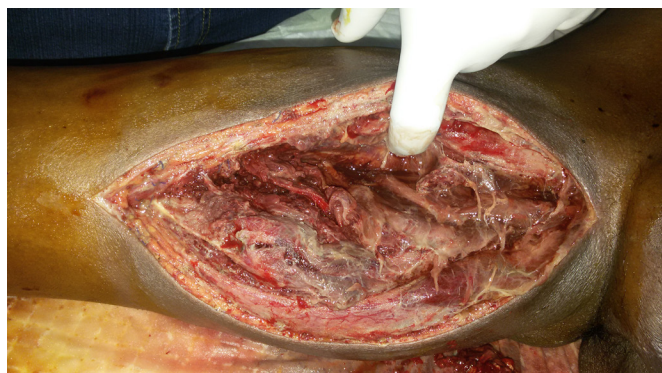


Figure 1 Fasciotomy and debridement showing necrotic muscles in adductor compartment.



Figure 3 Day 7 of treatment with topical CMS. CMS, colistimethate sodium.

carriers for local delivery of antimicrobial agents.² In view of high cost and worsening renal function, we tried a similar but cost-effective method of colistin therapy locally. One vial of CMS was mixed with a tube of debridase (15 g) ointment containing (pappain 521 700 IU+urea 100 mg) (Virchow Healthcare). Half of the mixture was applied over the wound per day after debridement and the remaining mixture was refrigerated and used the next day. We applied this mixture on the wound for 5 days working out to about 7000 INR for the patient. Patient responded well to the treatment (figure 3). His serum creatinine improved to 1.1 mg/dL. Subsequent culture sent for post-treatment showed no growth of organism. This was found to be a very cost-effective treatment modality.

OUTCOME AND FOLLOW-UP

The wound granulated well and healed (figure 2). He was sent home on anticoagulants for his DVT. He is being followed-up in the medical oncology department for his CML.

DISCUSSION

NF is a rapidly progressive severe soft tissue infection of the deep fascia that results in the destruction of overlying subcutaneous tissue and skin.³ NF affects people of all age groups but mostly in patients aged over 40 years.⁴ This infection can be difficult to recognise in its early stages and requires aggressive treatment to combat the associated high morbidity and mortality.⁵ Our patient is a case of type 2 NF of the lower limb with a poor prognosis due to MDR *K. pneumoniae*. The wound was treated locally by CMS, the prodrug of colistin converted to active form by hydrolytic enzymes present in the wound.⁶



Figure 2 Day 3 postfasciotomy—infected wound with slough.

With the emergence of MDR Gram-negative organisms, colistin has been considered as a potential therapeutic agent for the past 10–15 years.⁷ This has not only increased the clinical usage of this drug but also increased the prevalence of all the toxicities related to colistin. Colistin is known for neurotoxicities and nephrotoxicities.^{6,8} Colistin belongs to the class of polymyxins derived from *Bacillus polymyxa*. It exerts its action by disrupting cell permeability of Gram-negative bacteria.⁹ Colistin exists in two forms—colistin sulfate and CMS.

For the management of susceptible infections, colistin is given intravenously every 8 hours. In this patient, on account of local wound infection with a systemic response, fear of worsening renal function and economic concerns, systemic administration of colistin was considered to be irrational.

*Presence of hydrolytic enzymes in the wound site converts CMS to colistin by the hydrolysis of sulfomethyl peptide linkages.*¹⁰ Higher concentration locally with negligible systemic toxicity on local application is an added advantage here. In this patient, colistin was used as a powdered form. The bead form of colistin is available in the market,² but it was not used in this case due to the economic constraint on the patient. Though, theoretically, it is assumed that local use of CMS has no effect on bacteria, for this patient, we had a dramatic improvement in both eradication of the bacteria as well as in overall improvement in the patient condition.

Learning points

- ▶ In our case, the local application of colistimethate sodium over 2 weeks proved effective in eradicating multidrug-resistant *Klebsiella pneumoniae* associated with necrotising fasciitis.
- ▶ It can be a cost-effective treatment modality in selected patients in whom parenteral administration is toxic.
- ▶ Further research needs to be conducted to reveal the effect of local application of colistin in soft tissue infection.

Contributors SM: concept, acquisition, interpretation of data, drafting the paper and final approval. AVP: acquisition of data, revising critically and final approval. RR: concept, design, interpretation of data, revising critically for important intellectual content and final approval. All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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