Rehabilitation of a Rare Case: Successful Management of Hemophagocytic Syndrome

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Abstract

This report describes a case that presented to the department of Physical medicine & rehabilitation as a case of bilateral below –knee amputation, preceded by septicemia & gangrene. After a thorough evaluation & review of literature this case was diagnosed as Hemophagocytic syndrome, which is a potentially fatal hyper-inflammatory condition, characterized by an aggressive proliferation of activated macrophages and histiocytes that phagocytose hemopoietic cells [1]. This exaggerated immune reaction leads to prolonged fever, hepatomegaly, splenomegaly, skin rash, pancytopenia & coagulation disorders (features of HPS) [2]. HPS has been categorized into genetic or acquired. The acquired type may be associated with systemic juvenile idiopathic arthritis, autoimmune diseases; adult-onset still's disease, underlying malignancy & Ebsten's Barr Virus infection [2].

Keywords: Hemophagocytic syndrome (HPS), Adult onset Stills disease, Infective trigger, Amputation, Rehabilitation.

Case Presentation: A 20 year old African male student, 1 week prior to his admission presented with high grade fever in the A&E. He was suspected as a case of sepsis and was started on oral antibiotics. He was admitted to the local hospital 1 week after the initial presentation with high grade fever. In view of the additional findings of splenomegaly, abnormal liver function tests and a markedly elevated ferritin level which peaked to >75000 micro grams per liter, he was diagnosed with adult onset still's disease and prednisolone 50mg daily was started. Following admission, the pyrexia was ongoing and he clinically deteriorated with generalized body weakness & breathing difficulties.

Pseudomonas Aeruginosa was identified from the sputum and the urine. He was treated for sepsis with intravenous antibiotics. However within a week from admission, he became hemodynamically compromised & he went on to develop generalized tonic clonic seizures. CT and CSF examination was normal. Bone marrow biopsy revealed toxic features and proliferation of megakaryocytes. 3 days later, he developed pain in his limbs with weakening of his peripheral pulses. His immunosuppression was optimized with initiated IV Immunoglobulin.

He subsequently developed cold peripheries with absent peripheral pulse and diminished upper and lower limb reflexes bilaterally. Liver function tests were abnormal and there was a significant progressive elevation in ferritin levels. Blood results revealed anemia and thrombocytopenia. Anti-phospholipid screen revealed negative lupus anticoagulant, negative anti-cardiolipin & negative b-2 GPI-antibodies. The coagulation screen and blood screen were consistent with DIC. Auto-immune serology
was negative. Urinary examination revealed proteinuria & near normal serum creatinine.

Medical treatment consisted of management of sepsis & DIC with FFP, cryoprecipitate and anticoagulation, IVIG and steroids. However, within 48 hours his condition deteriorated again and he developed clearly demarcated dry gangrenous in both lower limbs distal to the knees. He consequently underwent bilateral below knee amputations in a single stage surgery. His post-surgical recovery was complicated by a wound just adjacent to the suture line. He suffered from further thrombotic episodes leading to skin necrosis of distal end of the right first and second digit of the hand.

Despite this, over the next 6 weeks he made good recovery & was hemodynamically stable. He was subsequently transferred to a tertiary hospital for active inpatient physical medicine and rehabilitation program of amputee rehabilitation. He was subjected to an intensive active rehabilitation program consisting of reconditioning exercises, a balanced diet, therapeutic positioning, stretching, stump bandaging, stump conditioning, intensive physiotherapy before prosthetic limb fitting.

Prosthetic prescription was at follows- Bilateral Transtibial endo skeletal modular prostheses with silicone liner suspension system, clutch Lock & dynamic foot. Post prosthetic fitting rehabilitation in form of donning & doffing training, gait training & ADL training was given for 4 more weeks. Towards the end of the rehabilitation programme he was walking in the parallel bar independently with upper limb support. He could don & doff the prosthesis on his own. Our goal being modified independence in ADL & successful reintegration back into the community.

Discussion

This is a rare complex case of a young man with adult onset Still’s disease, who presented with sepsis and went on to suffer with DIC resulting in infarction of his limbs. The main diagnosis considered was HPS and he met 6 of the 8 diagnostic criterions. To further support this diagnosis, he had an underlying infective trigger [3] consisting of uro-sepsis with Pseudomonas Aeruginosa.

Another diagnosis which was considered was the Catastrophic antiphospholipid syndrome, which is a potentially life threatening variant occurring in less than 1% of anti-phospholipid syndrome patients. The underlying pathology involves thrombotic microvasculopathy, which may lead to multiorgan failure & death in 30-50% of patients [4]. However, this was unlikely in this case, as lupus anticoagulant was negative & did not fulfill the diagnostic criterion for catastrophic Antiphospholipid syndrome [5,6].

Elevated serum ferritin is one of the hallmarks of HPS. It is also characteristically high in adult onset Still’s disease & often correlates with disease activity [7]. A specific challenge that we faced in rehabilitating this patient was that, early in the post-operative phase, he had developed a wound just next to the suture line. Wound was 2.5 by 1.5 cm. It was grade 2. Clean & non-infected, as the swab taken had come out negative. However, in this case the wound took a relatively long time to heal (Approx. 8 weeks). As a consequence we were unable to provide this patient early prosthetic fitting. So we waited till the wound has healed completely. The wound eventually healed. However, the wound healing was definitely prolonged in this case, which delayed prosthetic fitting by about 3 weeks.

Insipde of the initial deterioration & complexity of this case, this patient showed promising recovery and benefited significantly from a multidisciplinary active inpatient physical medicine and rehabilitation program. Timely multidisciplinary rehabilitation facilitated the reintegration of this patient back into the community inspite of sever disability. General precautions to prevent sepsis were warranted. This is one of the few reports of rehabilitation of a case of multiple limb amputation complicated by HPS in association with adult onset stills disease [8].

Conclusion

This case report highlights the following observations-
Amputee rehabilitation of a patient with a rare diagnosis of HPS.

In spite of early deterioration & complexity of the disease, timely multi-disciplinary active rehabilitation programme has resulted in good functional outcome.

The rehabilitation phase was complicated by prolonged wound healing which delayed early prosthetic fitting.

All precautions should be taken to prevent infections, as they can potentially trigger recurrent exaggerated autoimmune reaction.

Diagnostic Criteria for HPS: Criteria A or B Must be met for a Diagnosis

A. Molecular diagnosis consistent with HPS: pathological mutations of PrF1, unc, munc18-2, rab 27a, stx11, sh2d1a or Birc4or

B. 5/8 criteria

References


