Case Report -2

Multidrug therapy for Dapsone Resistant Disseminated Cutaneous Rhinosporidiosis

Jency Maria Koshy[1], Tony Mathew[2], S.K Mathew [1]
[1] Professor Department of General Medicine, [2] Associate Professor, Department of General Surgery, Believers Church Medical College Hospital, Thiruvalla, Kerala
Corresponding Author: *jencymkoshy@gmail.com*

Abstract:
Rhinosporidiosis is a chronic granulomatous infection caused by Rhinosporidium seeberi. We report the case of a 62 year old immunocompetent male who was diagnosed with Rhinosporidiosis 45 years ago. He was noticed to have a nasal swelling at the initial presentation. He continued to have recurrences of the nasal swellings for the next 38 years, for which he underwent surgical resections at least twice every year. Seven years ago, he started developing multiple cutaneous swellings. In spite of multiple surgical resections and oral dapsone, the lesions kept increasing in size and number.

He responded to sequential resection of the swelling and triple drug therapy with Cycloserine, Dapsone and Ketoconazole. He had a marked response to this new treatment regimen. Surgical resection has been the mainstay for treatment and dapsone was the only drug that was used earlier for this disease.

Cycloserine, Dapsone and Ketoconazole combination therapy could be a promising treatment in disseminated rhinosporidiosis non-responsive to dapsone. Key words: Disseminated rhinosporidiosis, Dapsone, multi drug therapy.

Introduction:

Rhinosporidiosis is a chronic granulomatous infection caused by Rhinosporidium seeberi.

A number of previous studies using various drugs like dapsone, ketoconazole, ciprofloxacin and amphotericin B suggested encouraging results only with dapsone.(1) We report the case of a patient who responded to the new treatment regime following clinical failure with dapsone.

Case report:

This 62 years old man from Kerala was apparently well until 48 years prior to admission when he developed swelling in the nose and headache. There was a history of swimming in a pond regularly for many years. He underwent biopsy of the nasal swelling and was diagnosed to have rhinosporidiosis. He was initiated on Tab Dapsone and underwent surgical resection of the mass. Thereafter he underwent repeated surgical excision of the nasal swellings, on an average 2 resections per year for the next 28 years since the swellings used to recur and block the nostrils. Seven years prior to his admission to our hospital he was noticed to have new lesions over the right thigh.

Thereafter over the next 2 years he developed swellings over the left thigh, left calf, left dorsum of the foot, left forearm,

bilateral arms, right upper back and right mammary area. He underwent resections of the right thigh swelling which later became ulcerated. He took Dapsone for 35 years with intermission in between.

When he presented to us he was noted to have pallor and multiple swellings over his body. He also had ecchymosis over this swelling and the swelling over the right thigh was ulcerated and had fluid oozing from the ulcer (Figure 1).

Figure 1:

Initial investigations revealed bicytopenia (Table1)with peripheral smear showing anisopoikiocytisis, schistocytes and normochromia. His Coagulation profile was normal.

Table 1: Hematological parameters of the patient.

Parameters	1st Day	2nd day	3rd day	4th day	7th day	14th day	4th weeks	2nd Mon	3rd Mon	5th Mon
Hb g/dl	10.8	-	-	-	10.8	10.9	10.7	9.7	11.6	11.3
TLC/mm^3	4800	-	-	-	9100	9200	10,100	5500	10,800	8800
Platelet/mm^3	46,000	66,000	52,000	42,000	74,000	85,000	1.32	1.07	1.6 L	2.6 L

(Hb- Hemoglobin, TLC- Total leukocyte count)

A biopsy of the swelling was done to reconfirm the diagnosis. Bone marrow aspiration and biopsy were also performed to look for bone marrow infiltration. His blood sugars were normal and HIV Elisa was negative. There was no evidence of any chronic liver disease on sonography.

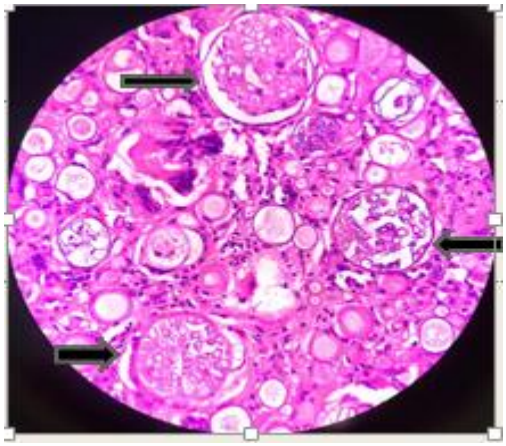

Figure 2:

Biopsy revealed numerous sporangia with endospores (Figure 2).

KOH smear also revealed sporangia with endospores and gram stain revealed gram positive sporangia. Bone marrow examination revealed normocellular marrow with normoblastic erythropoiesis, normal granulopoiesis and adequate megakaryocytes.

Since he was clinically resistant to Dapsone we had to look for an alternate therapy. In an earlier case report, there was a good response to therapy with Cycloserine, dapsone and ketoconazole in a seropositive patient.(2) We started Tablet Cycloserine 250 mg thrice a day, Tablet Dapsone 100mg once a day and Ketoconazole 400 mg once a day. He also underwent sequential surgical resections of the mass.

His thrombocytopenia reverted to normal within a month (Table 1).

He made marked improvement and gradual resolution of lesions while on treatment (Fig3).

Fig 3

He continued his treatment for 1 year and 11 months. However after stopping the therapy there were recurrences of lesions after 5 months. He underwent further resections and was restarted on Cycloserine, Dapsone and Ketoconazole.

Discussion:

Rhinosporidiosis is commonly seen in adult men and the possible mode of transmission is by direct contact with spores through dust and through swimming in stagnant water.(3) Rhinosporidium seeberi is an aquatic parasite.(4) Rhinosporidiosis can manifest in various forms as nasal, ocular, mucosal, cutaneous or disseminated.(5) Disseminated form as in this case is quite rare.

The presumed mode of infection from the natural aquatic habitat of the organism is through trans epithelial infection most commonly in nasal sites.(6) Mode of spread to other areas could be via autoinoculation, direct inoculation or haematogenous spread.(7, 8)

The types of skin lesions could be satellite lesions, in the skin adjacent to the nasal Rhinosporidiosis, generalised cutaneous type with or without nasal involvement as in this case or primary cutaneous type associated with direct inoculation of organisms onto the skin.(5, 9)

Dapsone was the only drug considered to

have an anti-rhinosporidial effect, which arrests maturation of sporangia and promotes fibrosis in stroma, when used as an adjunct to surgery.(10, 11)
Great caution should be exercised during surgical excision as it can lead to haematological dissemination which could have been the possible cause of dissemination in this case.

Multidrug regimens have been useful in diseases like tuberculosis and mycobacterium leprae Infections.(12) Clinicians have looked at the efficacy of multiple drug therapy in the treatment of Rhinosporidiosis. Arseculeratne proposed a multidrug therapy, combining dapsone with Cycloserine and other drugs that have been shown to have in vitro antirhinosporidial activity, for the treatment of rhinosporidiosis in order to delay the development of drug resistance.(13) George et al. treated a retroviral patient with multidrug therapy with Cycloserine, dapsone and ketoconazole.(2)

There was a significant response to this multidrug regimen in that patient with dapsone refractory disseminated rhinosporidiosis at the end of 1 year. Our patient also had a significant response with this novel multidrug therapy for disseminated rhinosporidiosis refractory to dapsone therapy. However, the duration of therapy is yet an unanswered question.

Conclusion:

Multidrug therapy with Cycloserine, Dapsone and Ketoconazole along with surgical resection has been shown to be promising in the treatment of disseminated rhinosporidiosis which is clinically refractory to dapsone therapy.

Limitations: Considering the disseminated presentation, he was screened for Diabetes Mellitus and HIV. However, he was not screened for any primary immunodeficiencies.

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