Mucormycosis is an aggressive, opportunistic fungal infection caused by organisms belonging to the class of Phycomycetes. Mucormycosis occurs almost exclusively in immunocompromised patients e.g. uncontrolled diabetics, those on chemotherapy and steroids. Rhino-occulo-cerebral mucormycosis (ROCM) is the commonest anatomical presentation of mucormycosis and is a potentially fatal disease. Despite advances in diagnosis and management, mortality rates are high. In a large series of 35 patients reported from Chandigarh, India, and in metaanalysis by Yohai et al, it was shown that survival rate declines as the interval from the onset of symptoms to the time of diagnosis increases.1,2 High degree of suspicion, early diagnosis and prompt aggressive surgical evacuation of the inflammatory material along with amphoterecin therapy can save lives as indicated by 75% cure rate in our current series.

Case Reports

Case 1
A sixty five years male, diabetic for 13 years and poorly controlled in spite of insulin therapy, was admitted with history of throbbing headache and pain in right eye of 4 weeks duration. At admission, he had watery discharge from right eye and purulent discharge from right nostril. Examination showed complete ophthalmoplegia and inflamed and edematous anterior chamber of right eye, tenderness over right maxillary sinus. Sino-scopy confirmed severely inflamed right maxillary sinus. Total WBC count was 12800 cells/cumm, random plasma glucose was 348 mg%, and serum creatinine was 1.2 mg%. Urgent CT scan of paranasal sinuses showed pansinusitis with erosion of floor and medial wall of the orbit. Urgent nasoendoscopy was performed and inflammatory material was evacuated and sent for smear, culture and histopathology. Smear showed aseptate hyphae with sporangiophores. Histopathological examination subsequently confirmed the diagnosis. IV infusion of amphoteracin was started after a test dose and based on weight and tolerance, daily dose was gradually increased. He tolerated amphoteracin very poorly and developed several side effects such as severe rigors, vomiting, sinus bradycardia followed by atrial fibrillation, in spite of very gradual increase in daily dose. Patient received a total dose of 589 mg of amphoteracin and at this stage repeat CT scan of sinuses showed considerable regression of soft tissue in paranasal sinuses. He took discharge on request at this stage. He has been very closely followed up for five years and is totally cured of ROCM.

Case 2
A 60 years farmer, diabetic for 5 years, was transferred from district hospital where he was admitted in diabetic keto-acidosis. He had history of throbbing left sided headache, pain and tenderness over left maxillary sinus area, and blocked left nostril. His total WBC count was 16400 cells/cumm, random blood glucose was 267 mg%, and serum creatinine was 2.8 mg%. Since he had not responded to IV ceftazidime and metronidazole started at the district hospital, ROCM was suspected and urgent CT scan of paranasal sinuses was done. Urgent nasal endoscopy was done. Left nasal cavity and left ethmoidal and maxillary sinuses were cleared of blackish material, which was sent for smear, culture and histopathological examination. Smear showed aseptate fungal hyphae. Subsequently culture grew mucormycosis. IV amphoteracin injection was started and dose gradually increased. He could tolerate only up to 1 mg/kg/day. Attempts to up titrate the dose resulted in side effects such as rigors, severe giddiness, and vomiting. He received a total of 1300 mg of amphoteracin. Repeat nasal endoscopy after three weeks showed complete clearance of inflammatory mass and smear was negative for fungi. Repeat CT scan of sinuses showed complete clearance. He has been followed up for two years and has been cured of ROCM.

Case 3
A 58 years female having type 2 diabetes for 4 years and not taking any antidiabetic medicines, was admitted with history of fever, headache and nasal discharge of 2 weeks. The discharge was initially serous and later became purulent with blackish tinge. Her endoscopy showed severe left maxillary sinusitis. The blackish discharge was collected and sent for smear, culture and histopathology. Her random plasma glucose on admission was 302 mg%, WBC count was 8700 cells/cumm, and serum creatinine was 0.6 mg%. Smear showed aseptate fungal hyphae
suggestive of mucormycosis. Subsequent histopathological report showed acute inflammatory lesion with fungal ball. CT scan of paranasal sinuses showed inflamed left maxillary sinus. IV amphotericin was started and dose gradually titrated. She showed rapid improvement and repeat sinoscopy done 6 days after starting amphotericin showed complete clearance of lesion. After receiving 626 mg of IV amphotericin she took discharge on request. At that time she had shown complete resolution of all the clinical manifestations. She has been regularly followed up for nine months and is cured of ROCM.

Case 4

A 70 years male, having type 2 diabetes for 2 years was admitted in toxic state with fever and severe pain and swelling in right eye with purulent discharge for four days. On examination, his general condition was poor. He had severe inflammatory changes in anterior chamber of right eye with total ophthalmoplegia and periorbital cellulitis. On endoscopy, his right ethmoid and maxillary sinuses were inflamed and filled with blackish material. His WBC count was 18000 cells/cumm, random plasma glucose was 615 mg%, urine and plasma ketones were negative. Serum creatinine was 1.6 mg%. Smear from nasal discharge showed aseptate fungal hyphae and culture grew mucormycosis. CT scan showed right ethmoidal and maxillary sinusitis and specks of air was seen in right maxillary soft tissue, and right infraorbital and infratemporal fossa. Within twenty four hours after admission and after controlling plasma glucose with IV insulin infusion, he was subjected to endoscopic sinus surgery under general anesthesia and all the inflammatory tissue and discharge was evacuated. Subsequently right eye was enucleated. He was put on IV liposomal amphotericin along with IV piperacillin–tazobactum combination. His general condition and neurological status deteriorated rapidly and by 72 hours after admission he required ventilatory support. He did not respond to treatment and died four days after hospitalization.

Discussion

Mucorales grow on decaying organic debris and occur worldwide in soil. Mucormycosis is an opportunistic infection which spreads by direct as well as haematogenous dissemination. It is a suppurative infection with vascular invasion resulting in thrombosis, embolism and infarction.

ROCM in poorly controlled diabetics carries high mortality. Seemingly trivial symptoms such as unilateral nasal blockage, discharge, and headache should not be ignored. Early clinical findings include nasal congestion and discharge, painful swelling of the orbit and face and proptosis, usually unilateral. Involvement of III, IV, VI and ophthalmic division of V cranial nerve is not uncommon. Clinical features often resemble those of cavernous sinus thrombosis. The cases described above had typical presentation. Their age ranged from 58 to 70 years. All had longstanding type 2 diabetes with poor metabolic control at the time of admission. The duration of symptoms ranged from four days to four weeks. High degree of suspicion, prompt diagnosis, availability of senior ENT and ophthalmic surgeons on emergency basis and good coordination between diabetologist and above mentioned surgical specialists, and aggressive medical (amphotericin, glycemic control) and surgical treatment (extensive debridement of the affected tissues] can give gratifying results as obtained in our series, where mortality was limited to twenty-five percent.

The exact dose of amphotericin for effective eradication of ROCM is not known. Western literature mentions 1 to 1.5 m/kg body weight daily till a maximum of 3 gm is reached. We observed that our patients require much smaller dose and their tolerance of conventional amphotericin is extremely poor. Two out of three patients who survived, had complete clinical as well as radiological resolution as assessed by CT scan by the time they received around 600 mg of amphotericin. At this stage both took discharge on request and were followed up on outpatient basis over a long term. Liposomal amphotericin, which is less toxic, is beyond the reach of most of them.

Points to Remember

ROCM is not uncommon in poorly controlled diabetics. One should keep it in mind and investigate patients with suggestive nasal and ocular clinical manifestations, particularly in those with poor control of plasma glucose. Early diagnosis and prompt medical and surgical management can save lives.

Total dose of amphotericin for complete eradication of ROCM is probably much lower than that mentioned in the Western literature.

References


ANNOUNCEMENT

API Orations / Lectureships

Recommendations are invited from members for the following assignments so as to reach, Hon. General Secretary – API, Dr. Sandhya Kamath by 31st July 2009.

Category No. (i) (General Medicine)
- Netaji Oration – 2010 & 2011
- Dr. G.S. Sainani Oration – 2010 & 2011
- Dr. PJ Mehta Oration – 2010 & 2011

The selected candidate has to deliver his/her lecture at the Annual Conference of API 2010/2011. The above orators will get the Award money of Rs. 10,000/- and TA for Orator by economy class airfare from API, complimentary registration and complimentary one night stay in the designated Conference hotel by the APICON Organising Committee.

Category No. (ii)
- Searle Oration - 2010 & 2011 (General Medicine)
- Prof. Rathinavelu Subramania Endowment Oration - 2010 & 2011 (General Medicine)
- Ranbaxy Oration - 2010 & 2011 (Infectious diseases)

The selected candidate has to deliver his/her lecture at the Annual Conference of API 2010/2011. The above orators will get the award money of Rs. 5,000/- and TA by economy class airfare from API, complimentary registration and complimentary stay in the designated conference hotel by the APICON Organising Committee.

Category No. (iii) : All lectureships viz

1. Dr. Coelho Memorial Lectureship in Experimental Medicine – 2010 & 2011,
2. Sinofi Aventis Lectureship in Diabetes – 2010 & 2011

The selected candidate has to deliver his/her lecture at the Annual Conference of API 2010/2011. The above lectureship will get the award money of Rs.5,000/- and TA by economy class airfare from API, complimentary registration and complimentary stay in the designated conference hotel by the APICON Organizing Committee.

For the above all lectureships and awards are open to eminent persons from the discipline of medicine and allied subjects such as Pharmacology, Biochemistry, Pathology and Physiology.

The selected candidate has to deliver his/her lecture at the Institution of his/her choice in the year 2009. The candidate has to get a notification in writing from the Institution that he/she has delivered the lecture.

Persons are selected from the recommendations received from members of the API. The orator in the discipline of medicine should preferably be a member of API. The recommendations for the above assignments must be accompanied with reasons for recommending a particular person showing the value of his/her research and eight copies each of three of his/her best publications. All relevant papers in connection with the suggestions, such as the bio-data, list of publications etc., should be submitted in 8 sets by the proposer. The recipient of the above oration should deliver a lecture pertaining to his/her work at the Annual Conference in January, 2010.

Those who have received Oration / Lectureship in a given category are eligible for application for the other two categories.

The members of the Governing Body of API and the Members of the Faculty Council of ICP are not eligible to receive any Oration, Lectureship or Award.

The prescribed nomination form for the above orations / Lectureship are on the API website “apindia.org”

The completed application forms for the above Lectureship should reach to Dr. Sandhya Kamath, Hon. General Secretary of API, Unit No. 6 & 7, Turf Estate, Opp. Shakti Mill Compound, Off. Dr. E. Moses Road, Near Mahalaxmi Station West, Mumbai - 400 011 not later than 31st July 2009.

Dr. Sandhya Kamath, Hon. General Secretary
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