left paranasal sinus, exenteration of the left orbit, removal of the brain lesion and maxillary resection with teeth extraction were gradually performed. After three months of this treatment, the progression of the fungal infection was finally stopped.

It can be concluded that intensive antifungal therapy together with extensive surgical intervention led to elimination of the infection and saved the patient's life. After more than four years of recovery from the infection, the patient lives a normal life; however, he is followed up by a haematologist as well as by plastic and dental surgeons and some reconstructive facial surgery is planned.

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P246 | Chronic pulmonary aspergillosis in a tertiary care center in Spain: A retrospective, observational study

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Objective: The aim of this study was to describe the characteristics of a cohort patients with chronic pulmonary aspergillosis (CPA) treated in a tertiary care center in Spain and analyze factors related to mortality.
Patients and methods: A retrospective cohort study of all patients diagnosed with CPA between January 2010 and December 2015 in a tertiary hospital in Spain was conducted. The patients were identified through the Microbiology Department registry. Patients with at least one respiratory culture positive for *Aspergillus*, one positive galactomannan assay in bronchoalveolar lavage (BAL) or one positive *Aspergillus* PCR in BAL meeting the diagnostic criteria for CPA (according to recently published guidelines) were included. Demographic, clinical, radiological and microbiological data were recorded, as well as clinical course and all-cause mortality at 3-, 6- and 12-months. Patients were followed up until death or loss to follow-up or until 30 June 2016. Univariate analysis was performed to assess the influence of different variables on 12-month all-cause mortality. Variables that were found to be statistically significant in univariate analysis were analyzed by multivariable logistic regression.
Results: Fifty-four patients were included. Among them, 25 patients (46%) suffered from COPD, 9 (17%) had lung interstitial disease and 19 (35%) had cancer, in 11 cases (20%) with primary or metastatic lung involvement. Eleven patients (20%) had a history of pulmonary tuberculosis and 4 (7%) a previous lobectomy. Twenty-four patients (44%) were receiving corticosteroids, 14 (26%) chemotherapy and 11 (20%) other inmunosuppresors. The most frequently identified radiological patterns were the chronic cavitary pulmonary form (CCPA) in 26 cases (7 with aspergilloma inside a cavity) and subacute invasive aspergillosis (SAIA) in 14 cases. In patients where culture was available (52), most frequently isolated species were *Aspergillus fumigatus* (34 cases), followed by *A. niger* (5), *A. flavus* (4) and *A. terreus* (4). Bronchoscopy was performed in 22 (40%) patients. Forty-three patients (80%) received antifungal treatment: voriconazole as initial treatment in 24 cases, itraconazole in 14, intravenous liposomal amfotericin B in 2, nebulized liposomal amfotericin B in 2 and anidulafungin in 1. Five patients received a combination of two antifungals. In 10 (19%) cases surgery was conducted. At 3, 6 and 12 months after diagnosis all-cause mortality was 39%, 46% and 56%, respectively. Independent predictors of 12-month mortality were active cancer (OR, 5.975; 95% CI, 1.32-27.09; $P = .02$) and previous pulmonary tuberculosis (OR, 0.65; 95% CI, 0.01-0.6; $P = .16$).
Conclusions: Our results provide data on clinical characteristics and outcomes of CPA emphasizing the role of comorbidities. Active cancer was related to higher mortality, while post-tuberculosis CPA was associated with lower mortality.

P247 | Rhino-orbital-cerebral mucormycosis in a diabetic ketoacidotic patient - case report

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Introduction: Mucormycosis is a rare but life threatening invasive mycosis caused by members of the Mucorales order. It usually develops in an immunocompromised host, mainly diabetics, but also in hematologic malignancies or transplanted patients. The usual clinical presentation of this fungal sinusitis is a combined rhino-orbital-cerebral infection and, despite the advances in combining antifungal and surgical treatment, it remains a fatal human infection in most cases.
Materials and Methods: Case report of a patient presenting with prostration and left eye exophthalmia and cellulitis, as a result of mucormycosis. We highlight the particularities of the surgical endoscopic debridement, microbiology and histologic results.
Results: 68 years-old male, with no prior relevant history, presented with a 2-day history of polydipsia, polyuria, prostration, fever and

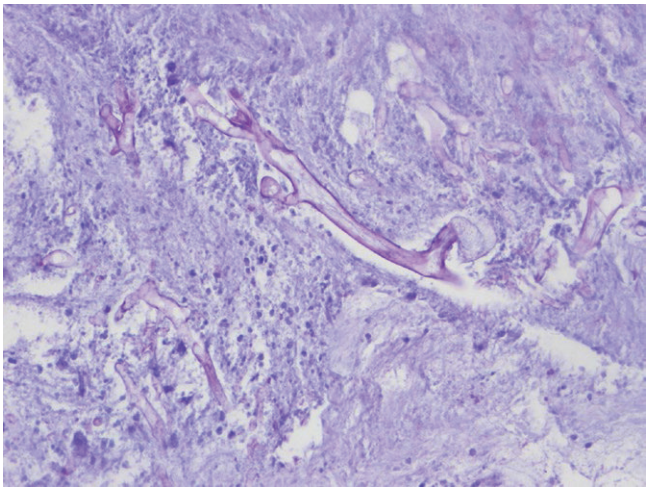

FIGURE 1 Histologic image (PAS 600x): multiple giant non-septate hyphae, surrounded by necrotic tissue and inflamatory cells.

dyspnea. Findings included left eye exophthalmia, chemosis and limitation on ocular movements. Laboratory results were compatible with an inaugural diabetic ketoacidosis and sinus and orbital-CT-scans showed a left side ethmoidalsinusitis, with postseptal cellulitis. Despite the metabolic correction and broad-spectrum antibiotic coverage, the neurologic status didn't improve and brain scans showed a diffuse hypointense frontobasal area compatible with an ischemic stroke and intracranial extension of the inflammatory process. Urgent endoscopic surgical debridement of the sinus infection was accomplished through an endoscopic total ethmoidectomy, maxillary, sphenoidal and frontal sinusotomy. Intraoperatory findings included a scarce purulent discharge and a diffuse necrotic sinus mucosa. The histologic and microbiologic results were compatible with an invasive sinus mucormycosis: broad non-septate hyphae were observed on direct examination of sinus biopsy. On culture, macro and micro characteristics were compatible with *Rhizopus arrhizus* and amphotericin B was started in high doses. Identification confirmed by sequencing of genomic DNA fragments proved to be a ***Rhizopus microsporus***. The initial post-operative period was favorable, with improvement on the left eye and sinus inflammatory signs but the neurologic status declined on the 4th day, with a huge hemorrhagic transformation of the frontal necrotic parenchyma ending in a fatal result. We present surgical images and video recording of the endonasal procedure, microbiology and histology pictures.

Conclusions: Despite the aggressive therapy, the fatal closure is, unfortunately, a common result of mucormycosis. The angioinvasive feature of *Mucormycetes*, enhanced by the ketoacidic pro-growth environment, causes a purulent arteritis and thrombosis with resultant ischemia and infarction of tissues. Intracerebral hemorrhage probably resulted from mycotic aneurysms rupture. Early diagnosis, combined treatment and reversal of the immunosuppressive status remain the key points to a successful result.

P248 | Fungal infections of the paranasal sinuses caused by fungi of the *Cladosporium* genus in a patient suffering from acute monocytic leukemia

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Introduction: Immunocompromised patients, especially those suffering from malignant disease are at risk for developing invasive fungal infections (IFI). Patients with acute myeloid leukemia are regarded as high risk for developing IFI. The most frequent causes of fungal infections are fungi of the genus *Candida* and *Aspergillus*. The fungi of the genus *Cladosporium* are ubiquitous and are the most common indoor and outdoor molds. Some species are plant pathogens, while others parasitize other fungi. *Cladosporium species* are rarely pathogenic to humans, but have been reported to cause infections of the skin and toenails as well as sinuses and lungs.

Objectives: The aim of this paper is to present case report of fungal infection of the paranasal sinuses caused by fungus of the genus *Cladosporium* in a patient with acute monocytic leukemia.

Methods: Case report and review of literature.

Results: Five-year old girl suffering from acute monocytic leukemia, developed the fourth episode of febrile neutropenia after the third block of intensive chemotherapy. Febrile neutropenia was unresponsive to first and second line empirical antibiotic therapy. Lung CT scan revealed pulmonary infiltrates, which was in correlation with early fungal markers in serum (positive anti-Aspergillus IgM antibodies). It was classified as a possible IGI and under suspicion of invasive pulmonary aspergillosis, voriconazole was started. After the fourth cycle of chemotherapy patient developed the fifth episode of febrile neutropenia, which was also unresponsive to empirical antibiotic therapy. Patient developed noticeable eyelid ptosis of the right eye and massive periorbital hematoma. CT scan of paranasal sinuses revealed expansive soft tissue formation in the right maxillary, nasal, and right sphenoidal cavity. Aspirate and sinus lavage fluid of maxillary sinuses were obtained and two types of mold were discovered. In two repeated and consecutive samples we have isolated fungus *Cladosporium*, and the treatment with liposomal amphotericin B was introduced for a period of four weeks. Control CT scan revealed near complete regression of lesions in the paranasal sinuses.

Conclusion: Mycological analysis of sinus lavage fluid and aspirate of the sinus can be significant for early diagnosis of rare fungal infections. This is the first case of fungal infection of the paranasal sinuses caused by fungi of this genus in our institution. In the extensive literature search, using key words: *Cladosporiim*, sinusitis and children's hematology, we did not find any case report of patient suffering from sinusitis caused by fungus of the genus *Cladosporium*.

P249 | Therapeutic target voriconazole level in children and adolescents with cancer: is it possible?

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Background: Voriconazole (VCZ) has a nonlinear pharmacokinetic profile and exhibits considerable variability in drug exposure. Therapeutic drug monitoring (TDM) may help to improve therapeutic response in patients with invasive aspergilosis, but evidences on clinical use of TDM in children are scarce.

Objective: Our aim was to evaluate whether it is possible to predict the therapeutic target from the usual recommended doses, in children with cancer undergoing chemotherapy.

Methods: Retrospective study performed at the Institute of Pediatric Oncology/Federal University of São Paulo, Brazil. All patients submitted to TDM for VCZ in the years 2016-2017 were included in the