Screening, Evaluation and Management of Invasive Fungal Sinusitis in the Immunocompromised Pediatric Patient

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Abstract

A retrospective case review was conducted to identify possible areas for improvement in a protocol in place at The University of Texas Southwestern Medical Center (UTSW) for the past ten years for which the Pediatric Otolaryngology service at a large tertiary care children’s hospital is evaluated to identify all neurotropic patients for febrile care with nasal endoscopy. All patients with nasal sinus magnetic resonance imaging (MRI) (ithnic on in chronic anatomic appearance evident) should undergo further evaluation, while those without suspicious nasal/lumens are followed up the next day to ensure no development of concerning symptoms. Any patient with a concerning lesion proceeds to operative endoscopy with biopsy. If pathologic tissue evaluation demonstrates IFI, all inpatient and outpatients appearing tissue that can be safely removed is debrided. Antifungal therapy is initiated, and at least one additional follow-up operative nasal endoscopy is performed depending on extent and aggressiveness of the disease.

Results and Discussion

Of the 176 patients consulted to ORL for suspicion for IFI, 82 were female and 94 male. 41 had B-cell ALL, 19 had T-cell ALL, 18 had AML, and 28 had recently undergone bone marrow transplant for AML and ALL. 19 had T-cell ALL, 8 had bone marrow transplant for AML, and 16 had hematopoeitic malignancy.

176 consultations since 2013 were reviewed at UTSW utilizing billing data for Otolaryngology consultation with a concurrent diagnosis of fungal neutropenia. Seven of the subjects had biopsy proven IFI. The cases were reviewed and analyzed to glean descriptive clinical information with the goal of constructing a decision matrix to improve pre-test probability prior to patients undergoing nasal endoscopy, an invasive and uncomfortable procedure which causes considerable distress to patients and is associated with additional healthcare costs for the episode of disease. In our patient population, all subjects were female, but not all were neutropenic. Neutropenia was not an independent predictor of IFI as determined by operative nasal endoscopy with biopsy, nor was any particular etiology of immunocompromise. None of the patients with biopsy proven IFI were younger than five years old, but in the multivariate analysis, younger age was found to be a significant protective factor. Likewise, gender did not affect risk of IFI. The presence of any particular hallmark heralding symptoms of IFI such as rhinorrhea, epistaxis, nasal congestion or crusting, or facial pain or swelling was not independently predictive of IFI, but having at least one of these symptoms was a statistically significant predictor. Additionally, unexpectedly, patients with abnormal flexible nasal endoscopes had a high likelihood of a positive biopsy once taken for operative evaluation.

An abnormal nasal endoscopy had a high sensitivity (100%) and 90% specificity for IFI, with a positive predictive value of 54% and a negative predictive value of 100%. The presence of at least one of the constellation of associated symptoms including epistaxis, nasal or facial pain or swelling, rhinorrhea or nasal crusting was highly sensitive (99%) for IFI, but not very specific (44%), with a low positive predictive value of 7%. However, of clinical significance there was 100% negative predictive value – no a lack of any associated symptoms in our study population negated this could be considered a rung of the clinical algorithm leading to more invasive measures such as endoscopy. No particular presenting or associated symptom was associated with a higher likelihood of disease. Although neutropenia did not reach statistical significance as a predictor of IFI status, the negative predictive value was 100%. This indicates immunocompromised individuals in our population may have been protected against the disease, which adheres to our understanding of the natural history of the disease.

The presence of infection in any form is first identified by the patient’s history. A more thorough physical examination by history, physical examination, and radiographs is completed, with a close attention paid to any possible rhinologic injury or trauma. Once a patient is suspected of having the disease, an urgent request for an MRI of the head is given to the radiology department. If the patients consults, 24 were not neutropenic, and 35 had ANC > 500. Most of these had a history of neutropenia in the past, with fever > 5 days. All of the biopsy proven cases of IFI had symptoms in addition to febrile neutropenia. One of the biopsy proven IFI cases was referred because of imaging findings suggestive for sinonasal fungal infection in addition to febrile neutropenia. Retrospectively, it was noted that this subject had facial pain 5 days prior to the date on which the CT chest was obtained. The etiology of immunocompromise was not significant in these patients who were immunocompromised, with no difference being detected between AML, ALL or BMT, or other causes.

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Existing UTSW Protocol

Patient: Neutropenic + febrile ≥ 5 days

Action: Otolaryngology consultation with flexible bedside nasal endoscopy

Key Parameters P-value Lower 95% Upper 95%

Male Gender 0.792839 -0.07926 0.006823
Age > 5 years 0.133271 -0.01842 0.116861
Fever > 5 days 0.169519 -0.02264 0.126986
Neutropenia 0.430657 -0.22384 0.253258
Neutropenia > 5 days 0.363662 -0.00663 0.001782
ANC < 500 0.190281 -0.23010 0.040300
Undergoing chemotherapy 0.599034 -0.06822 0.100748
B-cell ALL 0.753344 -0.03811 0.529697
T-cell ALL 0.894095 -0.10246 0.118891
AML 0.781909 -0.39466 0.523587
BMT 0.503070 -0.29373 0.379307
Other etiology of immunocompromise

Sym- Rhinocerebral/epatatis 0.583923 -0.07161 0.128677
Sym- Nasal congestion 0.477551 -0.05797 0.127315
Sym- Nasal crusting 0.306308 -0.11902 0.108426
Any Symptoms 0.042628 0.001211 0.087059
Abnormal scope 0.229457 -0.042407 -0.09785

Table 1: Multivariate analysis of factors possibly predictive of IFI

Methods

A retrospective case review was conducted using billing codes for ENT consults in a patient with diagnosis of febrile neutropenia during the same episode of care to identify subjects. 170 patients were identified since 2011 and their charts were analyzed for data including duration of fever prior to consult, nadir of neutropenia, gender, age, anemia, treatability, comorbidities, disease process, clinical presentation, bedside exam findings, operative findings and culture results. These data were analyzed using the Fisher’s Exact Test and both univariate and multivariate regression in a combination of Microsoft Excel and SPSS. Relative risks were also computed.

Conclusions

Recommendation: Based on our data, extreme vigilance must be cultivated for any symptom suggestive of IFI in the context of febrile neutropenia, and the presence of symptoms warrants prompt endoscopic exam at the bedside to ascertain need for biopsy.

Evaluation and diagnosis require invasive procedures including nasal endoscopy and biopsy that can generally be performed in an adult, but often require general anesthetics in a pediatric patient with incumbent risks in an already fragile patient. However, with development of fungal endoscopy including multi-parametric imaging for sinonasal endoscopy, there is a growing trend towards developing endoscopes with enhanced imaging properties. For young children undergoing magnetic resonance imaging, as well as considerable monetary costs associated with this imaging. However, occasionally poor quality scope exams can lead to delayed diagnosis. The results demonstrated that the development of IFI most commonly caused by Aspergillus, Rhizopus and Bipolaris, which can rapidly develop to widespread destruction of the sinonasal cavity before evacuation and necrotic appearing tissue that can be safely removed is debrided. Antifungal therapy is initiated, and at least one additional follow-up operative nasal endoscopy is performed depending on extent and aggressiveness of the disease.

The prevalence of symptoms as a pre-terminal marker for increased mortality of IFI cases has been repeatedly reinforced as a poor prognostic factor, and early detection is key.

References