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INSTRUCTIVE CASE

YOUR DIAGNOSIS PLEASE: 8-YEAR-OLD CHILD WITH CHRONIC EAR DISCHARGE, INFRAORBITAL ULCER, AND PNEUMONIA

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CASE PRESENTATION

An 8-year-old female consulted at our institution due to left ear discharge. 6 months prior to consulting, the patient developed infraorbital swelling and erythema after she hit a metal post. The site of trauma eventually developed into a 2 x 2 cm abscess, which spontaneously ruptured. She was given cloxacillin for 7 days with no improvement of symptoms. 4 months prior to consulting, she developed foul-smelling left ear discharge, not associated with pain. She was given unrecalled otic drops and oral medications with no improvement. She eventually developed left facial paresis. Due to the persistence of ear discharge, she was brought to a local clinic where she was diagnosed to have chronic suppurative otitis media (CSOM) and referred to our institution.

The patient also had an 8-month history of a recurrent cough and weight loss of 10% over 3 months. She had no history of fever, seizure, or change in sensorium. She has an older sibling who is an ongoing 2nd month of anti-tuberculosis treatment. She was given BCG vaccination at birth. Her nutritional status is poor, with meals consisting usually of instant noodles, rice, bread, and cookies.

The patient was admitted for evaluation and management. On physical examination, she was awake but in respiratory distress. She was tachycardic and tachypneic, with a heart rate of 144 beats per minute and a respiratory rate of 50 counts per minute. Her oxygen saturation was 96% at room air. She was severely wasted and stunted, with a weight of 12.6 kg and a height of 106 cm. She had a 2 x 2 cm erythematous ulceration lesion with purulent discharge at the left lower eyelid, and a 5 mm lagophthalmos of the left eye. She had yellow, foul-smelling discharge on both ears, with 10% central perforation of the left tympanic membrane and a near total perforation of the right tympanic membrane. She had multiple cervical lymphadenopathies. She had crackles on bilateral lung fields, with mild subcostal retractions. Heart sounds were distinct. The abdomen was soft, with no organomegaly noted. Aside from her left peripheral facial palsy, the rest of the neurologic exam was normal (Figure 1).

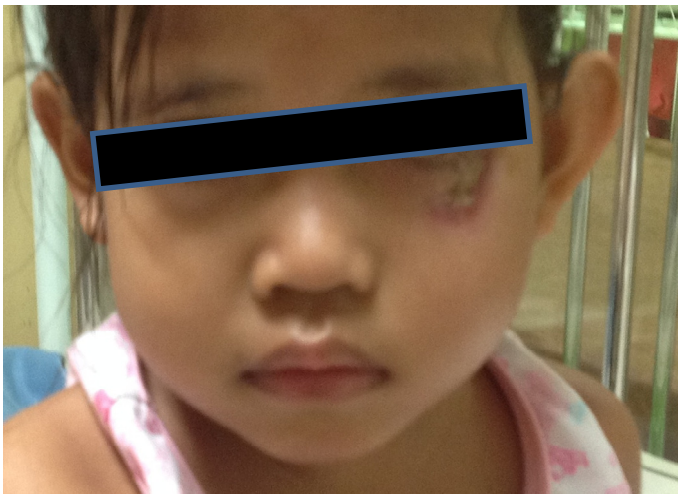
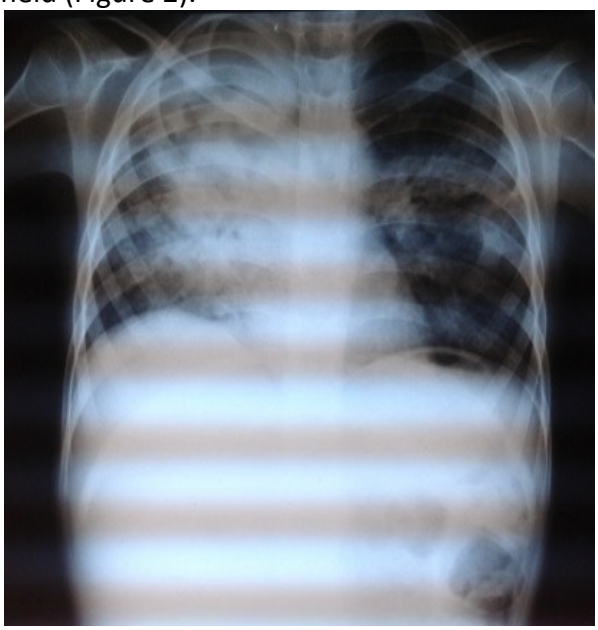


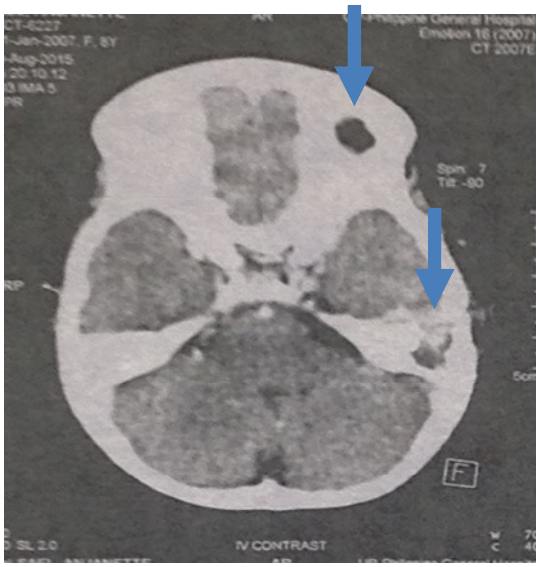
Figure 1. 8-year-old female with ulcerated left lower eyelid and left facial palsy

Complete blood count showed leukocytosis with neutrophilic predominance and thrombocytosis. The WBC count was 19, with 60 percent segmenters. The platelet count was 1152.

Chest radiography showed hilar lymphadenopathy and infiltrates at the right lung field (Figure 2).



Holoabdominal ultrasound revealed multiple hepatic foci with parenchymal disease, the largest measuring 1.7 x 1.7 x 1.4 cm. Cranial computed tomographic (CT) scan showed extensive osseous lytic changes in the left mastoid bone, with soft tissue component measuring 1.2 x 2.5 x 1.1 cm. Similar lytic changes were noted in the left orbital wall (Figure 3).



What is your diagnosis?

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DENOUEMENT

An 8-year-old female presented with a 6-month history of infraorbital swelling, which spontaneously ruptured and ulcerated. She then developed painless, foul-smelling otorrhea with left facial paresis. She had a chronic cough and weight loss and had an older sibling with tuberculosis. Tuberculin skin test was positive at 41 mm. Gastric acid-fast bacilli (AFB) smear showed +1 AFB. Ear discharge culture studies revealed very few colonies of coagulase-negative staphylococcus species, which was regarded as a contaminant. Ear discharge AFB smear was negative, but ear discharge TB polymerase chain reaction and gene Xpert was positive for TB. Pure tone audiometry showed severe hearing loss of the left ear and moderate hearing loss in the right ear.

The patient was diagnosed with disseminated TB involving the lungs, bone, ear (TB otitis media), skin (ocular scrofuloderma), and liver, with severe acute malnutrition. She was started on isoniazid, rifampicin, pyrazinamide, and ethambutol, and referred to the gastrointestinal service for upbuilding. She was also given cefuroxime for pediatric community acquired pneumonia. She was discharged well, with stable vital signs and steady weight gain.

DISCUSSION

Tuberculosis (TB) is a ubiquitous disease caused by the pathogen *Mycobacterium tuberculosis.* It affects millions of adults and children worldwide, and most commonly manifests as pulmonary TB. In rare instances, atypical manifestations of TB may be encountered and may cause a diagnostic dilemma.

KEYWORDS: Tuberculosis; disseminated TB; TB otitis media, scrofuloderma

The global burden of disease of TB is tremendous, with an estimated incidence of one million children per year[1]. TB of the ear is rare, representing just 0.04 percent of all cases of CSOM[2]. Based on a local retrospective study done in 2011, only 12 patients with TB otitis media were seen at a tertiary hospital in Manila from the years 2004 to 2009[3].

TB otitis media usually occur secondary to pulmonary TB, with the spread of the TB bacilli through the Eustachian tube. Hematologic spread may also occur [2]. The classic triad of TB otitis media is painless otorrhea, multiple tympanic perforation, and facial palsy, all of which were present in our patient. The otorrhea in TB otitis media predictably fails to respond to the usual antimicrobial treatment, as illustrated also in our patient[4].

Diagnosis is commonly delayed due to low diagnostic suspicion and the painless nature of the disease. This may result in severe complications, including deafness, ataxia, cranial nerve palsy, and intracranial abscesses or tuberculomas. In our patient, facial nerve palsy and hearing loss was present at the time of consult. Some authors recommend that painless otorrhea in patients with TB should be considered tuberculous in origin in order to minimize delay in diagnosis[5].

Ocular scrofuloderma is extremely rare. According to a study conducted in India, less than 40 cases of ocular scrofuloderma has been described so far[6]. It is usually unilateral and starts as a small nodule which can ulcerate eventually. It is commonly associated with pain, as well as mucoid or purulent discharge. Ocular scrofuloderma is acquired through hematogenous spread or by direct infection of a break in the skin of the eyelid due to trauma[7]. In our patient, direct infection of the eyelid secondary to trauma was most likely the culprit.

Table 1. Summary of the strengths and limitations of the WHO endorsed diagnostic modalities for tuberculosis

Diagnostic Tool	Strengths/Limitations
Microscopy	Least expensive and most rapid test Overall sensitivity of 20-50% Has a poor positive predictive value of 50-80% in settings where nontuberculous mycobacteria are common, such as the Philippines
Culture	Sensitivity: 80% Processing of results takes 4 to 6 weeks
Xpert MTB/RIF assay	Used for screening, diagnosis, and detection of rifampicin resistance Sensitivity: 97.0% (95% CI 95.8-97.9) Specificity: 48.6% (95% CI 45.0 -52.2) The poor specificity precludes its use for monitoring TB treatment and should not replace standard smear microscopy and culture
Line probe assay	Sensitivity 96% (CI 90% - 98%) Specificity 99% (CI 95%-99%) Positive predictive value 99% (CI 95-99%) Negative predictive value 95% (CI 89%-98%) Detects resistance to rifampicin and isoniazid in smear-positive sputum specimen

A case report of ocular scrofuloderma in a child was published in India recently, with distinctive similarities with our patient. The patient exhibited a 9-month history of poor weight gain, poor appetite, and bilateral infraorbital swelling. He had positive TB exposure and a positive tuberculin skin test of 20 mm. His aspirate AFB and TB culture were positive, while his chest radiograph was normal. His cranial CT scan showed osseous lytic and sclerotic changes. He was started on an anti-tuberculosis regimen. Marked improvement was noted after 2 months of treatment, with only a hyperpigmented scar observed on the right lower eyelid.

The diagnostic modalities for TB that are currently endorsed by the World Health Organization (WHO) include conventional microscopy, fluorescence microscopy. culture-based technologies, Xpert MTB/RIF assay, and line probe assay. The gold standard for the diagnosis of TB is culture, but the most prevalently used diagnostic examination is smear microscopy[8].

Table 1 summarizes the strengths and limitations for each of the endorsed diagnostic tools[8, 9, 10].

A study investigated the use of the T-cell activation marker—tuberculosis assay (TAM-TB assay) for the diagnosis of active TB in children. This was a proof-of-concept study conducted at the Ifakara Health Institute and the NIMR-Mbeya Medical Research Center in Tanzania. The premise of the study was that TB in children is still difficult to diagnose due to the non-specificity of symptoms, difficulty in acquiring adequate respiratory specimens, and the paucibacillary nature of the disease. This study aimed to evaluate the accuracy of this novel immunodiagnostic assay.

The TAM-TB assay relies on the immunological phenomenon observed during TB infection, which is the loss of expression of the cluster of

differentiation (CD) 27 surface marker in mycobacteria specific CD4+ T cells.

The study included 130 children who consulted from May 2011 to September 2012 due to symptoms suggestive of tuberculosis. Sputum samples for TB culture and blood samples for TAM-TB assay were obtained.

Results of the study showed that the TAM-TB assay was able to detect 15 out of the 18 culture-confirmed tuberculosis cases. 5 culture-negative patients were also identified by the TAM-TB assay to have highly probable TB. The sensitivity of the assay was 83.3%, with a 95% confidence interval of 58.6 to 96.4%. The specificity was 96.8%, with a 95% confidence interval of 89.0 to 99.6 percent. Moreover, test results were available within 24 hours after sampling, while culture studies had a median time of diagnosis of 19.5 days.

The authors of this study concluded that TAM-TB assay allows for easier specimen collection and shorter waiting time for results. However, further studies are still needed to obtain final validation[1].

The standard of treatment for tuberculosis is still isoniazid, rifampicin, pyrazinamide and ethambutol (HRZE). Our patient was advised to complete 12 months of treatment (2 months HRZE and 10 months HR) due to osseous involvement.

A common limitation of the standard regimen is non-compliance of patients due to the prolonged duration of therapy, which is closely linked to the development of resistant strains of *Mycobacterium.*

A phase 2 study evaluated the efficacy and safety of a new treatment regimen consisting of pretonamid, moxifloxacin, and pyrazinamide (Pa-M-Z) in drug sensitive and multi-drug resistant TB.[11] The primary endpoint was the rate of change in colony forming units (CFU) from sputum samples over a period of 8 weeks. Participants with newly diagnosed smear positive drug sensitive TB were randomized to receive HRZE or Pa-M-Z. Participants who received the Pa-M-Z regimen were divided into 2 subgroups. In 1 subgroup, 100 mg of pretonamid was given (Pa100-M-Z), while the other subgroup was given 200 mg (Pa200-M-Z). Patients with drug resistant tuberculosis were given the Pa200-M-Z regimen. Serial 16 hour pooled sputum samples for CFU counts were collected over 2 months.

Results of the study showed that all patients who received the experimental regimen had greater average reductions in CFU counts compared to HRZE, but only those received the PA200-M-Z regimen had a statistically significant decrease. Patients who received the Pa200-M-Z regimen also had significantly shorter median time to the first negative culture at 28 days, compared to the median time of 35 days for those receiving standard treatment.

Compared to the standard 6 month TB regimen, the novel PA-M-Z regimen is proposed to be given for four months only. Following the favorable results of this initial study, the Global Alliance for TB Drug Development is set to launch a bigger phase 3 trial known as the Shortening Treatment by Advancing Novel Drugs trial[11].

Conclusion

Tuberculosis remains to be a global epidemic, affecting millions of adults and children worldwide. While pulmonary TB remains to be the most common clinical manifestation, atypical presentation of the disease are occasionally observed, particularly in the pediatric population. A thorough history, physical examination, and a strong index of suspicion will aid the clinician in reaching a timely and accurate diagnosis. Early diagnosis will allow for prompt institution of management and prevention of complications. It is also important to keep abreast with advancements in diagnostic and therapeutic strategies, so that optimal care may be delivered to all patients with tuberculosis.

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