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Extensively drug-resistant Haemophilus influenzae invasive disease: Two fatal cases of vaccine failure

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Case Report

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Abstract

Background

The emergence of extensively drug-resistant *Haemophilus influenzae* strains is a serious global problem. *Haemophilus influenzae* type b (Hib) which was rare earlier in the post-vaccine era is becoming common. Invasive Hib disease cases are now observed even in countries with high Hib vaccine coverage, which raises the issue of vaccine failure. Mortality could be high in severe disease, especially in debilitated patients with drug-resistant strains.

Case report:

Herein we report two fatal cases of invasive *Haemophilus influenzae* b disease caused by extensively drug-resistant strains in fully vaccinated children. The first case had pneumonia and pericarditis which evolved to septicaemia and septic shock. The second case was admitted with sepsis complicated with severe meningitis and status epilepticus. Both patients had severe acute malnutrition.

Conclusions

These two cases illustrate a variety of clinical presentations of invasive Hib disease in fully immunized children under 5 years of age. Extensively drug-resistant Hib strains are emerging. In low-income settings, severe acute malnutrition could be a major predisposing factor to vaccine failure. Hence, a high index of suspicion for Hib infection is still required irrespective of the patient's vaccination status, especially in the presence of a debilitating condition. Early detection and management are paramount to reduce morbidity and mortality associated with invasive Hib disease.

Introduction

Haemophilus influenzae is a gram-negative coccobacillus that commonly colonises the upper respiratory tract (1), and is responsible for various infections, typically in the under-five children, the elderly, and the immunocompromised (2). Based on the capsular composition, *H. influenzae* can be classified into six different serotypes (a to f). The acapsular strains are referred to as nontypeable *H. influenzae* (NTHi) (3). Both capsulated and noncapsulated strains of *H. influenzae* are responsible for invasive infections. Invasive *Haemophilus influenzae* type b (Hib) disease is defined as a severe illness such as pneumonia, meningitis, septicaemia or septic arthritis, with isolation of Hib from a normally sterile site (4). Hib vaccine failure is considered when invasive Hib infection occurs ≥ 2 weeks after one Hib vaccine dose administered after the first birthday, or ≥ 1 week after ≥ 2 doses, given at less than 1 year-old (5). Hib, considered the most virulent serotype among the typeable strains, can impact several organs (6, 7).

According to the World Health Organization (WHO), Hib accounts for 3 million cases of invasive disease and 400,000 deaths annually worldwide (8). Even more so, Hib represents 3% of all-cause mortality in children under 5 years of age (9). The incidence of invasive disease seems to increase with immunocompromising medical conditions such as antibody deficiency, asplenia, neoplasms, hemoglobinopathies and HIV disease.

In unvaccinated children, Hib accounts for 95% of all cases of invasive *H. influenzae* infections (8). Introduction of Hib vaccines in the national programme of several countries has significantly impacted the epidemiology of infections, with a dramatic decline of invasive disease and mortality associated with *H. influenzae* type b (10). As a result, the incidence of invasive *H. influenzae* infections due to non-Hib strains, especially nontypeable *H. influenzae*, and serotypes a, e, and f, has been rising globally (11). However, invasive Hib infection is yet to be eliminated in areas with low vaccine coverage; and countries with high vaccine coverage still experience some sporadic outbreaks. In other words, even with effective Hib vaccination, invasive Hib infection cases can still occur (12).

Beta-lactams are the drugs of choice in *H. influenzae* infections. However, drug resistance to beta-lactams has emerged, and has evolved to other commonly used drug classes including fluoroquinolones, chloramphenicol, sulfonamides, and macrolides (13–15). Amid this growing concern over extensive drug-resistance among *H. influenzae* strains, carbapenems or drug combination therapies could be the last resort to be considered (16). Extensively drug-resistance is defined as resistance to at least one agent in all but two or fewer antimicrobial categories, that is, resistance to at least one agent in five or six antimicrobial categories (17).

To date, only few cases of extensively drug-resistant (XDR) *H. influenzae* have been reported, to the best of our knowledge. Herein we report two cases of invasive disease caused by an extensively-drug resistant Hib strain in fully vaccinated children, which resulted in the death of the patients. This is the first report of XDR *H. influenzae* in Malawi.

Case report

Case 1

A 1 year 2-month-old male patient was admitted at the Paediatric Emergency Unit with a history of fever and cough for 7 days, diarrhea and poor feeding for 14 days. He was treated for malaria twice in the previous 12 days at the health center where he was also followed-up for severe acute malnutrition (SAM). He was up-to-date with the immunization program and received Hib vaccine at 6 weeks, 10 weeks, and 14 weeks of age as part of the pentavalent vaccine formulation. The HIV status was negative. There was no history of seizures or impaired consciousness.

On admission, he was fully conscious and he weighed 7.6 kg. Records showed that he had lost 1 kg within 3 months. He was wasted, pale, febrile with temperature 38.7%, tachypneic at 60 breaths per minute (bpm), tachycardic at 176 beats per minute (bpm) and had cool extremities with signs of

dehydration. Oxygen saturation was 84% on room air. Chest and neurology examination were normal. He had a hypoglycaemia of 40 mg/dL, and anaemia with a hemoglobin level of 6.2 g/dL.

He was initially managed on supplemental oxygen, IV dextrose and blood transfusion. Samples were sent for culture, the blood panel and parasitology studies. Empirical antibiotic treatment with benzylpenicillin and gentamicin was commenced for a presumptive community-acquired pneumonia. The patient was then transferred to the Paediatric High Dependency Unit (HDU) for continued acute care and nutritional management. His complete blood count revealed a leucocytosis of 27,000/μL with a slight lymphocytic predominance (12,000/μL). Malaria parasites screening was negative. On the following day, the patient had no more stool losses, but had persistent fever and cough. There was now reduced air entry on the left lung. The IV fluids were stopped and the patient was switched to oral rehydration solution.

On day 3 of admission, the patient's condition deteriorated with increased work of breathing. His chest X-ray showed a complete opacification of the whole left lung in keeping with lung consolidation. Chest ultrasonography demonstrated a 1.3cm pericardial effusion, which was deemed not large enough to warrant a drainage. The patient was switched to continuous positive airway pressure (CPAP) and covered with intravenous flucloxacillin for a suspected invasive staphylococcal infection. A nasogastric tube was placed for nutrition. However, as of 4:10 pm, his clinical condition continued to worsen, with increasing respiratory distress. He became lethargic, had weak pulses and declining blood pressures. A venous blood gas was done immediately and showed respiratory acidosis. CPAP was continued at maximum settings; the shock was managed with intravenous fluids and inotropic support. Meanwhile, his preliminary blood culture revealed Gram negative bacilli, and the antibiotic therapy was upgraded to meropenem. Despite this management, the patient's condition continued to deteriorate, with severe respiratory distress, refractory shock and evolving bradycardia. Noteworthy, IV adrenalin which was started at 1ml/h at 4:10 pm was increased to 2 ml/h at 7:30 pm, then to 3 ml/h by 11:30 pm with fluid bolus up to 10 ml/Kg. At 1:40 am, the patient had a cardiorespiratory arrest. Cardiopulmonary resuscitation was undertaken for 20 minutes including bag mask ventilation, chest compressions, and one round of adrenalin, but without success. Death was confirmed, on day 3 after admission. It was only on the following day that the blood culture results became available, and showed growth of *Haemophilus influenzae* type b, sensitive to meropenem only, but resistant to ampicillin, ceftriaxone, chloramphenicol, ciprofloxacin, trimethoprim-sulfamethoxazole, penicillin, and tetracycline. The patient was declared to have died from invasive Hib infection with pneumonia, pericarditis and septic shock.

Case 2

An 8-month-old female infant was admitted with two weeks of intermittent fever and vomiting, as well as a few days of generalized tonic-clonic convulsions and altered consciousness. The history reveals that she was managed home with paracetamol for 9 days before seeking care at the nearest health facility. At the clinic, the patient had reportedly received one dose of an unspecified injectable antibiotic. Subsequently the family had absconded from the clinic and had gone home where they administered an

undisclosed traditional therapy for 5 more days despite consistent fever with on and off seizures. Upon the severity of seizures, and occurrence of altered consciousness, recurrent seizures and worsening of symptoms, the family finally decided to bring the child to our hospital.

This was a previously well-child with no significant past medical history. She had been born at term via spontaneous vaginal delivery at a peripheral health facility, and the mother died soon after due to postpartum haemorrhage. The weight at birth was unknown. The child was up to date with immunisation and development had been normal. The Hib vaccine was administered at 6 weeks, 10 weeks, and 14 weeks of age in the form a pentavalent vaccine. There was no other significant history.

On admission, the patient was comatose, scoring 1/5 on the Blantyre Coma Score (18), and had continuous generalized seizures. She looked pale, wasted with weight-for-length z-score < -3 standard deviations, and had signs of severe respiratory distress. There was no oedema. She had mild pyrexia (T: 37.7°C) and a severe tachycardia of 212 bpm. She was well perfused, and the rest of the examination was nonremarkable. Initial respiratory support was achieved noninvasively with nasal high-flow cannula at 5L/min. The seizures were first managed with IV diazepam 0.25 mg/kg. Two doses were given but seizures could not be controlled. Phenobarbital IM 20 mg/kg was started, but could not control the seizures either. The patient was then shifted to levetiracetam 30 mg/kg via nasogastric tube which also served for enteral feeding. However, the status epilepticus persisted.

The patient was then transferred to the ICU for intubation and management of status epilepticus. Initial investigation results showed a metabolic acidosis, leucocytosis of 38,500/μL, thrombocytosis of 1190.10^3/μL and microcytic anaemia (Hemoglobin at 6.5 g/dL, and mean corpuscular volume at 70.6 fL). A central nervous system infection was therefore suspected, and the patient was empirically started on high dose ceftriaxone and acyclovir, and given a packed red blood cells transfusion. Seizure control and sedation were achieved with phenobarbital 20 mg/kg, escalated to levetiracetam 30 mg/kg, and ketamine infusion 2 mg/kg IV.

Investigations suggested a meningoencephalitic involvement: Cerebrospinal fluid (CSF) analysis showed pleocytosis with polymorphonuclear cells predominance, 960 cells/μL with 92% polymorphs. An electroencephalogram (EEG) demonstrated non-specific changes consisting of extremely low amplitudes, and a lack of variability and reactivity, suggestive of an encephalopathic process. Computed tomography (CT) scan done on the second day after admission showed generalised cerebral oedema and a mild obstructive hydrocephalus (Figs. 1, 2 & 3). Both CSF and tracheal aspirate Xpert MTB/RIF were negative.

On the third day after admission, both blood and CSF culture samples sent prior to antibiotic administration grew *H. influenzae* type b which was resistant to all tested antibiotics except for meropenem and amikacin. The patient was immediately switched to meropenem. Supportive management was continued. However, the patient continued to deteriorate. On day 4 after admission, she had a cardiorespiratory arrest and died.

Discussion

Haemophilus influenzae type b can cause a range of invasive infections including pneumonia, meningitis, purulent pericarditis, sepsis, septic arthritis, and osteomyelitis (19), with children, the elderly and the immunocompromised being particularly at risk (18). Pericarditis and osteomyelitis are less frequent presentations. Acute bronchitis and otitis media caused by *H. influenzae* are usually associated with nontypeable strains. Hib is only involved in 5–10% of *H. influenzae*-associated otitis media (7). Pneumonia is particularly more common in developing countries (20). Meningitis is the most common presentation of Hib invasive infection (7).

Hib is a colonizer of the nasopharynx. The mechanism of bloodstream invasion remains unknown. A contributing factor may be a viral or mycoplasmal infection involving the upper respiratory tract. From the bloodstream, the pathogen can invade distant sites, especially the meninges (7). The pathogenesis of *H. influenzae* meningitis in children is different when compared to an adult. Whereas in adults contiguous spread is the principal mechanism, in children, hematogenous dissemination of the pathogen leading to seeding of the meninges is thought to be the common route of meningitis (21). Signs and symptoms of Hib meningitis cannot be distinguished from other bacterial meningitis. Hib meningitis case fatality rates vary. From 5% in developed countries, they could reach 40% in developing countries despite appropriate antimicrobial therapy. Survivors have high risk of developing sequelae, 10–15% of whom have severe complications such as bilateral sensorineural deafness, blindness, epilepsy, cerebral palsy, and hydrocephalus (8). Sepsis is the second most common clinical manifestation of Hib invasive disease and accounts for almost 25% of all confirmed cases of Hib invasive disease (8).

Among unvaccinated children, the highest incidence of Hib invasive disease is in the 6–24 months age group. This is because of the presence of protective maternal antibodies before 6 months, and the strengthening of natural immunity after 24 months of age (8). Invasive Hib infection was once common prior to the introduction of effective immunization (22). With the introduction of effective Hib vaccination, the incidence of Hib infections including invasive disease has dramatically waned worldwide, with an estimated regression in the incidence rate of more than 90% (12). In developing countries, it was demonstrated that Hib vaccine reduced all-cause mortality by up to 5% among children aged less than 5 years (9). In Malawi, a study assessing Hib vaccine impact in the prevention of Hib-associated meningitis in children < 5 years noted a decrease of Hib meningitis annual incidence, from 20–40 per 100,000 to near zero following vaccine introduction (23).

Although some existing data suggests that Sub-Saharan African countries (except for Gambia and South Africa) using a 3-dose Hib vaccine with no booster dose have not experienced a resurgence of invasive Hib infection, in many countries, a lack of effective surveillance may mask possible limitations of the vaccine's real impact in settings with high HIV seroprevalence or low vaccination rates (9). Several reports point toward a global resurgence of Hib invasive infection, even among countries with high vaccine coverage.

Surveillance in Argentina covering the 2011–2019 period reported 577 *H. influenzae* infection cases where Hib alone represented a burden of 41.1% of cases, with a considerable increase in the rates of type b, from 31.2% in 2011 to 50% in 2015. The proportion of cases attributable to vaccine failure among Hib cases was 1.4% (24).

In Portugal, where 4 doses of Hib are administered, and a vaccination coverage of > 95% is achieved, a national surveillance over 12 years revealed a significant increase of the incidence of invasive Hib cases. Vaccine failure rates also increased, from 13.5% in the first half of the study to 22% of all invasive Hib cases in the second half. Of the 41 reported cases of invasive Hib disease, 26 (63%) were vaccine failures. Seventy-three percent of the cases were children < 5 years of age (25).

In France, despite high Hib vaccination coverage, a consistent increase in the number of invasive Hib disease cases was noted between 2017 and 2019, with 25 cases recorded in 2019 only, bringing the tally to 56 cases in 3 years. Of these, twenty-four cases (43%) were associated with vaccine failure. The highest incidence of invasive Hib disease and vaccine failures was among children under 5 years of age. Of note, meningitis was the most common presentation (26). In the Netherlands, there were 9.4 cases of vaccine failure occurring annually on average between 2015 and 2019. In 2020, the rates increased to 10 cases, and by August 2021, ten new cases of vaccine failure were already recorded. The incidence was the highest among children aged 1–4 years (27). A surveillance in South Africa recorded an increasing number of invasive Hib infection cases in children 5 years, from a detection rate of 0.7 in 2003 to 1.3 cases per 100,000 children 5 years in 2009. The proportion of invasive disease cases classified as vaccine failure increased, from 43% in 2003–2006 period to 58% in 2007–2009 (28). A large-scale study involving 10 European countries, Israel and Australia also reported several cases of vaccine failure despite high levels of immunization coverage, including booster doses given in some of the countries (5).

The two cases presented in this article were between 6 months and 2 years of age, pointing to the vulnerability of children within this age group. The Hib conjugate vaccine was introduced in Malawi in February 2002 as part of a DTwP-Hib-HepB pentavalent vaccine formulation. The pentavalent vaccine protects against diphtheria, tetanus, whole cell pertussis, hepatitis B and *H. influenzae* type b, and is given at 6, 10 and 14 weeks of age (29).

Some research has been conducted to assess the impact of Hib immunization in Malawi using indirect methods (23, 30, 31). However, the real impact of the Hib vaccine could not be effectively assessed due to incomplete data. A more inclusive national survey assessing all – or at least most of – Hib-associated invasive diseases prevalence would best reflect the status of Hib pentavalent vaccine efficacy within the country. More importantly, to the best of our knowledge, data on national vaccine failure rates are not available in several countries including Malawi. This is a gap that needs to be addressed. Thus, predisposing factors need to be fully assessed in an African context to be able to draw conclusions.

The factors leading to vaccine failure are not clearly established. While Gilsdorf (9) and Ladhani et al. (5) mentioned some risk factors in children exhibiting vaccine failure, Marques et al., in a nationwide survey

in Portugal, failed to identify any clear predisposing factors that could warrant an intervention (25). Further, a national surveillance in England found that almost all children with invasive Hib disease had previously been healthy, and the disease had several clinical presentations (32). Based on the data from Gilsdorf, 44% of children experiencing vaccine failure at the age of < 1 year had either a clinical risk factor (such as prematurity, Down syndrome, developmental delay, neutropenia, or malignancy) or an immunodeficiency, or both; and two-third of children with vaccine failure at > 1 year of age, had either a clinical risk factor, or an immunodeficiency or both. Children with no predisposing factor who expressed Hib vaccine failure showed higher concentrations of anti-polyribosylribitol phosphate antibody after Hib infection than healthy control children, but with much lower antibody avidity. Gilsdorf postulated that inadequate immunological priming of polysaccharide antigens could be the mechanistic theory (9).

Amid these conflicting explanations, we present cases of children with underlying severe acute malnutrition. Research has found that severely malnourished children present several defects in their immune system, including increased gut permeability, thymic atrophy, reduced B-lymphocytes, effector T-cells, dendritic cells, mucous secretory IgA, microbicidal activity of granulocytes, complement factors, gastric acid production, and Th1 cytokines (IL-2, IL-12, IFNγ), with a weak vaccination titer response (33). A tentative explanation to unravel the connexion between malnutrition and immunocompromise suggested that deficiency in key micronutrients such as vitamins and oligoelements could be the cause (34). However, the pathophysiology behind immunological alterations in malnutrition are still unclear. It cannot be explained solely by deficiency in proteins, vitamins, and minerals since many other immune components are paradoxically elevated in malnutrition (35). Infections, environmental, hormonal and epigenetic factors seem to play a role in the immunocompromise and poor response to vaccine in severe malnutrition (33).

New evidence support that vaccine efficacy in malnourished children is determined by an interaction between three factors including immune function, nutritional status, and environment factors (36). The management of severe malnutrition requires therefore a holistic approach addressing these three determinants in order to achieve optimal levels of seroconversion (36, 37). Studying the kinetics of protective antibodies titers in severe malnutrition would provide more insights on the need to consider the inclusion of booster doses of available vaccines in the management of severe malnutrition. In Kenya, a Cochrane review showed that children with acute malnutrition who received a booster dose of the measles vaccine significantly improved in their antibody titers to reach levels comparable to those of well- nourished children (38). Beside the efforts to improve immune status, ameliorating environmental parameters involves promoting good sanitation and access to clean water (36). To complete the tripod, nutritional supplementations in zinc, iron, and vitamins A/C/D would be a considerable addition to the other two strategies aiming at the optimization of the management of severe malnutrition in LMICs (39).

One of our patients developed purulent pericarditis. This is a rare presentation of Hib invasive disease. This underlines the need for clinicians to have a high index of suspicion of invasive *H. influenzae* disease even if data suggests completion of immunization schedule.

Extensively drug resistant Hib strains, even though rare, have been reported in other countries (16, 40, 41). We report two cases of XDR Hib isolates which showed resistance to all the drugs tested on the Haemophilus susceptibility panel, which included ampicillin, ceftriaxone, chloramphenicol, trimethoprim-sulfamethoxazole, penicillin, and tetracycline as per the EUCAST 2025 Guidelines (42). A second panel of drugs was tested specifically for this case, and included meropenem, amikacin, erythromycin, and pefloxacin. These drugs are not used in the first line against *H. influenzae* infections in our institution and hence not routinely included in the antimicrobial susceptibility testing for *H. influenzae*.

For the second-line panel, the isolates from case 1 showed resistance to erythromycin, ciprofloxacin, and amikacin, and were only susceptible to meropenem. The Hib isolates from case 2 showed at least sensitivity to amikacin in addition to meropenem, and were resistant to the other two drugs. Development of such severely drug-resistance suggests that some complex drug-resistance mechanisms might be involved (16).

These results show that carbapenems may be the choice last resort antimicrobials in severely-drug resistant *H. influenzae* infections in our setting. *H. influenzae* seems to demonstrate regional distribution in serotypes and drug resistance patterns. The profile of *H. influenzae* susceptibility to commonly used antibiotics has changed considerably as a result of the widespread use of antibiotics (43). Drug-resistant *H. influenzae* (including XDR) tend to be more common in severe infections (20). Both cases discussed here came from the Blantyre region, and presented with severe Hib disease compounded by previous healthcare exposure. These factors may have contributed substantially to the development of XDR Hib strains in these patients. The question to elucidate is whether these XDR Hib strains are intrinsically invasive and then gain resistance mechanisms or whether XDR status confers invasive abilities to these strains. We did not perform whole genome sequencing of the isolates to investigate on their relatedness, which is a weakness in this case report.

Whereas reports point towards an alarming rise in beta-lactamase producing Hib strains, which have nearly doubled from 2003 to 2023 (20), an increase in the non-enzymatic mechanism, that is gene mutations strains, has also been noticed recently (4). We additionally tested for ESBL production using the cefpodoxime-clavulanic acid (CPD, 10µg/1µg)/cefpodoxime (CD, 10µg) combination disk method. (44). Both isolates were not ESBL producers, meaning that other mechanisms of resistance were involved. As these strains were not *βeta*-lactamase producers, but resistant to ampicillin, they were therefore classified as *βeta*-lactamase negative, ampicillin-resistant (BLNAR).

Western countries like France, Poland, Sweden, Portugal, and Spain have all reported rising prevalence of BLNAR *H. influenzae* strains, ranging from 12.8% in Poland to 56% in Spain (21). According to current literature, BLNAR strains are associated with a high risk of treatment failure due to their increasing resistance to *β*-lactam antibiotics. This threat calls for continuous surveillance of the prevalence of BLNAR strains among *H. influenzae* infection (45). Additionally, it is crucial to evaluate antimicrobial susceptibility patterns and track the resistance trends of *H. influenzae* in order to inform local antibiotic prescription decisions, thereby lowering the risk of treatment failure (46).

Therefore, it is paramount to implement robust antimicrobial stewardship policy to control the emergence and/or spread of XDR *H. influenzae*, and to prevent acquisition of ESBL among *H. influenzae* strains as *H. influenzae* was included on the World Health Organization's priority pathogen list for which new antibiotics are urgently required (10).

Sadly, our two patients died within 72 hours of hospitalisation, after suffering severe invasive infections. Despite HDU and intensive care, the outcomes could not be improved and both patients eventually demised. Late hospital presentation contributed significantly to this poor outcome.

Conclusion

Invasive Hib infection can still occur in settings with high Hib vaccine coverage, and can result in a fatal outcome in both unvaccinated and vaccinated children who experience vaccine failure. A high index of suspicion is needed even in fully vaccinated children, particularly those with chronic debility and immunosuppression. Acute severe malnutrition could be one of the main predisposing factors to Hib vaccine failure in developing countries. Extensively drug-resistant Hib strains are a major global concern for which strict antimicrobial stewardship should be applied in health facilities. Their occurrence worsens the prognosis considering the long turnaround for culture and sensitivity results required for antibiotic therapy tailoring. Active surveillance programs need to be implemented to track circulating drug-resistant strains of *H. influenzae* serotypes, and report cases of vaccine failure for optimal management.

Abbreviations

BLPAR: β-lactamase-positive ampicillin-resistant

CD: cefpodoxime-clavulanic acid

CPAP: continuous positive airway pressure

CPD: cefpodoxime

ESBL: Extended-spectrum *βeta*-lactamase

H. influenzae: *Haemophilus influenzae*

Hib: *Haemophilus influenzae* type b

HIV: human immunodeficient virus

MDR Multidrug-resistant

MTB/RIF: *Mycobacterium tuberculosis*/rifampicin (resistance)

NTHi: nontypeable *Haemophilus influenzae*

PBP3: penicillin-binding protein 3 (PBP3)

WHO: World Health Organization

XDR: Extensively drug-resistant

Declarations

Ethics approvable and consent to participate

Not applicable.

Consent for publication

A written informed consent was obtained from the parents for publication of these cases and any accompanying pictures.

Availability of data and materials

The images supporting the findings of these cases are included within the article.

Competing Interests

All authors declare no conflict of interests.

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Authors' contribution

ENM was responsible for the colligation of the cases drafts, and the manuscript writing. ZM and NB drafted the case 1 report. TE and JN drafted the case 2 report. CK interpreted the CT scan images. CMK performed microbiology culture and antimicrobial sensitivity testing. DK interpreted the cultures and antimicrobial sensitivity testing results. KK revised the manuscript. All authors read and approved the final manuscript.

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Figures

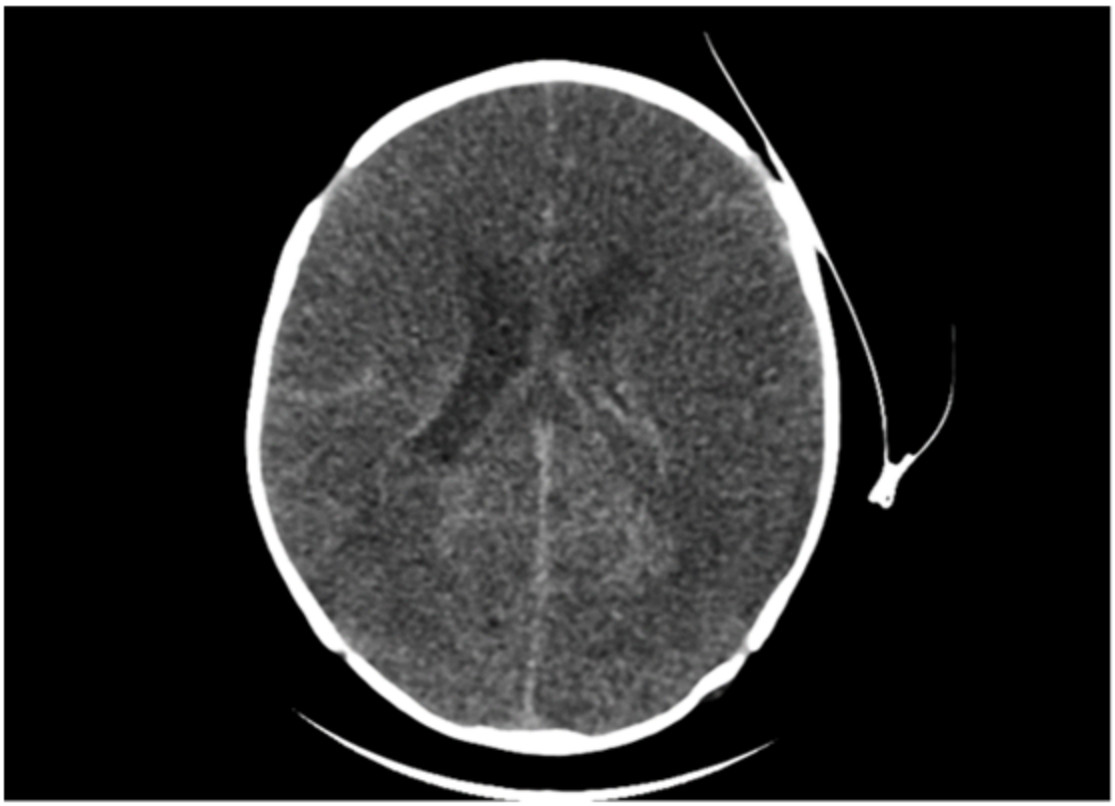


Figure 1

Cerebral oedema: Complete effacement of sulci, hypodense appearance of the brain with loss of normal grey/white matter differentiation on a CT scan.

Source: Authors

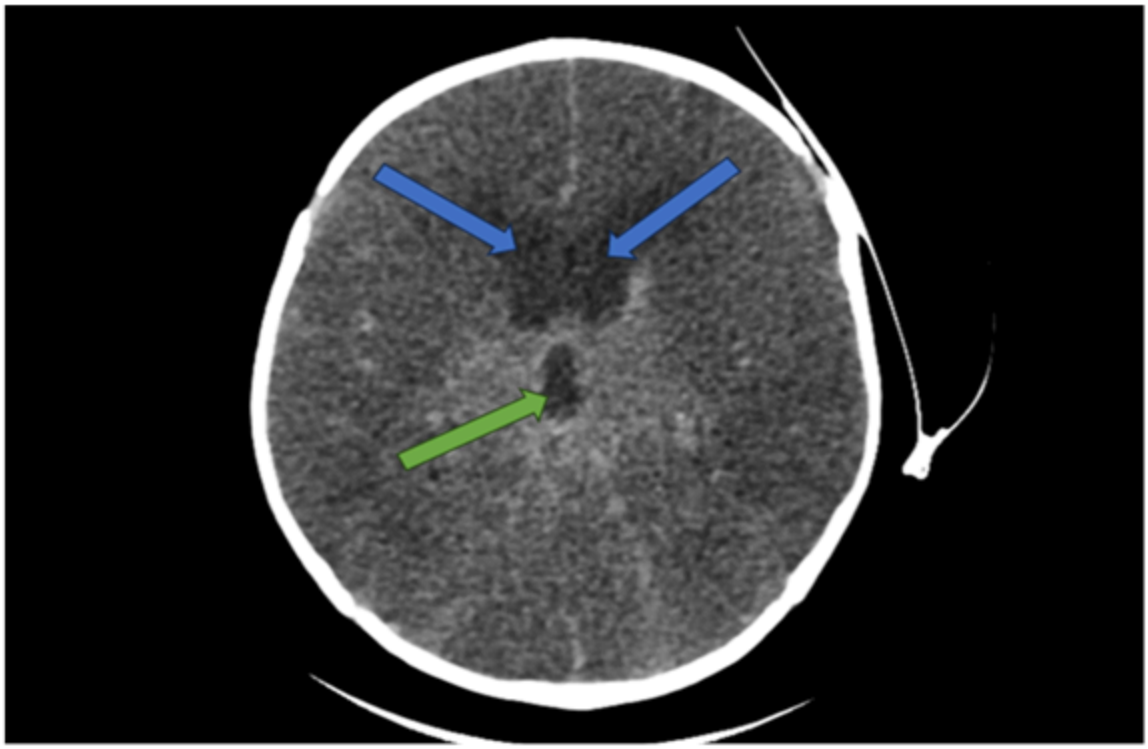


Figure 2

Hydrocephalus as a complication in a patient with meningitis: Enlarged lateral ventricles (blue arrows) and third ventricle (green arrow) on a CT scan.

Source: Authors

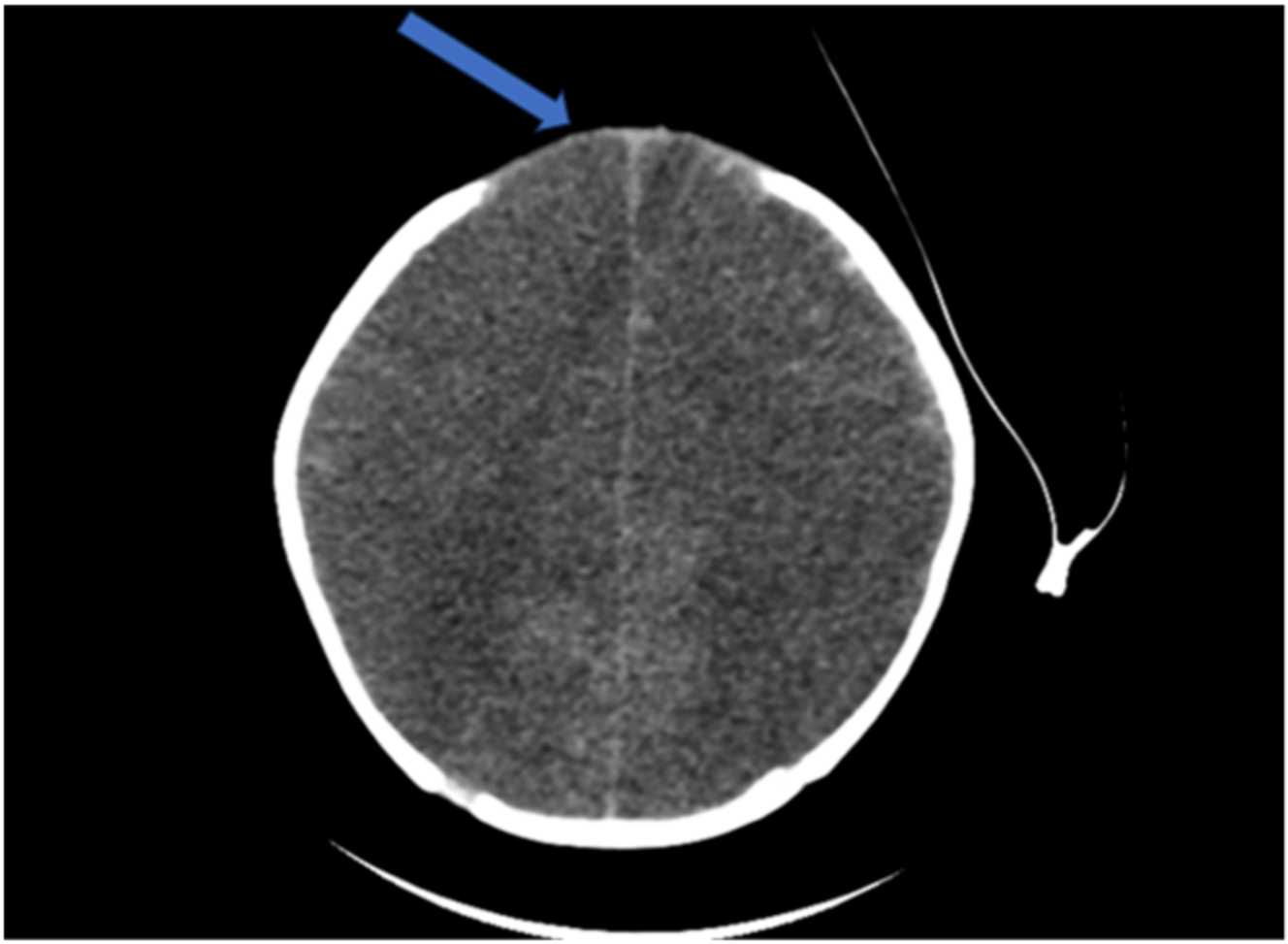


Figure 3

Hydrocephalus with widening of the anterior fontanelle and the sutures (blue arrow) shown on a CT scan.

Source: Authors