Rare disease

Strongyloides hyperinfection syndrome following resection of meningioma

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Summary

In this report, we present the case of a patient who developed the strongyloides hyperinfection syndrome 3 weeks after an uneventful resection of a sphenoid wing meningioma. She originally presented with symptoms of raised intracranial pressure and was given dexamethasone before surgery. The pathology, diagnosis and management of *Strongyloides stercoralis* are reviewed.

BACKGROUND

This case of the strongyloides hyperinfection syndrome highlights the importance of considering this rare diagnosis in immunosuppressed patients at risk of chronic strongyloidiasis.

CASE PRESENTATION

A 41-year-old woman of Paraguayan origin, who had been living in Europe for several years, was referred to the emergency department of our district hospital by her general practitioner. She had a 3-day history of headache, nausea and deteriorating mobility and a 1-day history of diarrhoea and vomiting. She was found semi-comatose on the morning of her admission.

The patient had presented a month earlier with symptoms of raised intracranial pressure and was diagnosed with a large left sphenoid wing meningioma. She was given oral dexamethasone and underwent an uneventful Simpson grade II resection of a grade I meningioma. Her symptoms improved after surgery and she was discharged 5 days later on a tapering steroid regime.

On examination, she was agitated with a positive Kernig's sign. She had a respiratory rate of 34 and SpO₂ 77% on oxygen via a non-rebreathe mask (FiO₂ ~0.85); on auscultation, her chest was clear. Her heart rate was 140 bpm, blood pressure was 85/66 mm Hg and the Glasgow Coma Scale (GCS) score was 9/15 (M5, V2, E2). She had generalised abdominal tenderness and a non-blanching haemorrhagic peri-umbilical rash was noted.

INVESTIGATIONS

An initial arterial blood gas analysis showed a mixed metabolic and respiratory acidosis with relative hypoxaemia (FiO₂ 0.85, pH 7.18, pO₂ 17.5 kPa, pCO₂ 6.3 kPa, base excess -9.8 mmol/l). Her full blood count indicated normocytic anaemia (haemoglobin 7.7 g/dl, mean cell volume 94 fl) and a marked neutrophilia (white cells 22.4×10^9 /l, neutrophils 18.3×10^9 /l). The eosinophil count was within the reference range.

A provisional diagnosis of meningoencephalitis was made, and the patient was given intravenous cefotaxime and vancomycin following discussion with the microbiologist. A noradrenaline infusion was commenced and the patient was intubated and ventilated.

A CT of the head showed modest cerebral oedema within the middle cranial fossa and a liquefying haematoma, consistent with the patient's recent surgery. A CT of the abdomen showed non-specific jejunal wall thickening and a filling defect in the superior mesenteric vein, consistent with evolving small bowel ischaemia. Bilateral pulmonary consolidation was noted. The suspicion of abdominal sepsis secondary to small bowel ischaemia was raised and the patient was transferred to the operating theatre and underwent an exploratory laparotomy that demonstrated normal small and large bowel. She was subsequently transferred to the intensive care unit where a lumbar puncture was performed and treatment for meningitis, comprising antibiotics, antivirals, glycaemic control, haemodynamic and respiratory support, was continued.

Cerebrospinal fluid microscopy showed gram-negative rods and an analysis of the cerebrospinal fluid (CSF) was consistent with bacterial meningitis (white cells 2500×10^6 /l, neutrophils 30%, protein 1.87 g/l, CSF: plasma glucose <0.4). Over the following 3 days, CSF and blood cultures were both found to be positive for *Escherichia coli*. Gentamicin was added to the antibiotic regime.

TREATMENT

The antibiotic regime was continued, vasopressors were weaned off and sedation breaks were introduced; however, the patient showed little neurological response. Transfer to the regional neurosurgical centre for further assessment and expert management was arranged.

OUTCOME AND FOLLOW-UP

On arrival at the neurosurgical centre, the patient remained in a poor neurological state with a GCS score of 3/15 when the sedation was withheld. Imaging of the

brain showed multiple areas of low density in both hemispheres and in basal ganglia with obliteration of the basal cisterns, suggesting multiple infarcts due to raised intracranial pressure.

Following admission to the neurosurgical intensive care unit, the patient developed bloodstained diarrhoea. Gastric endoscopy showed a gelatinous material partially obstructing the duodenum; stool microscopy revealed *Strongyloides stercoralis*. Subsequently, larvae were also isolated in the CSF. She was found to be negative for HIV and human T-cell lymphotropic retrovirus (HTLV-1) antibody. The infectious disease team confirmed the diagnosis of strongyloides hyperinfection syndrome associated with immunosuppression from steroids and a veterinary preparation of parenteral ivermectin was administered. Despite treatment, the patient deteriorated further and subsequently died a few days later.

DISCUSSION

Strongyloidiasis is most commonly a consequence of infection with the soil dwelling nematode *S stercoralis*. There are thought to be approximately 100 million cases of strongyloidiasis worldwide and it is considered endemic in tropical and subtropical climates, particularly sub-Saharan Africa, South and Southeast Asia, Central and South America with smaller areas of the USA and Eastern Europe affected.¹ *S stercoralis* is unique among intestinal nematodes in its ability to persist within the human host for many decades with the potential to cause life-threatening disease associated with immunosuppression.

The life cycle of *S stercoralis* is complex with both a free-living and a parasitic phase. The free-living cycle begins when non-infective rhabditiform larvae are passed in stool. In soil, these larvae may develop into either infective filariform larvae or adult free-living worms, which produce eggs that hatch into rhabditiform larvae. In the parasitic cycle, filariform larvae in the soil penetrate the skin (usually the intact skin of the foot) and migrate to the lungs. Subsequently, they ascend the pulmonary tree and enter the gastrointestinal tract where they develop into adult female worms in the small bowel mucosa. These adult female worms produce eggs that hatch into rhabditiform larvae which, in turn, are passed in the stool to start the free-living cycle. Alternatively, an auto-infective cycle may be established if the rhabditiform larvae develop into filariform larvae within the bowel and the host is re-infected by invasion of the intestinal wall or perianal skin.^{2 3}

The clinical features of strongyloidiasis are variable and often subclinical. The initial infection is often asymptomatic but symptoms described include a seriginous urticarial rash at the site of skin penetration by the infective larvae followed several days later by cough and tracheal irritation as the larvae undergo pulmonary migration.⁴ Chronic infection is usually asymptomatic but larva currens (a local urticarial rash with a moving, linear component caused by intermittent larval migration) and gastrointestinal symptoms, such as abdominal pain, bloating, diarrhoea and constipation, are commonly reported.^{4 5}

Strongyloides hyperinfection and disseminated infection are rare and the outcome is poor with a mortality of up to 87%.⁶ In hyperinfection, the parasite load is

increased but restricted to organs usually involved in the life cycle. Hyperinfection may manifest with gastrointestinal symptoms including bleeding, abdominal pain, diarrhoea, anorexia, weight loss and small bowel obstruction. In addition, pulmonary symptoms including cough, wheeze, respiratory failure and pulmonary haemorrhage may be present. In contrast to chronic strongyloides infection, eosinophilia is rare in hyperinfection. As in this case, dissemination can occur in hyperinfection and affects organs not usually involved in the life cycle.⁴ Hyperinfection and dissemination may be complicated by gram-negative septicaemia due to translocation of bowel organisms.^{3 5} *E coli* meningitis is a recognised complication of strongyloides hyperinfection.⁷

Hyperinfection and dissemination usually occur in the immunocompromised host. HTLV-1 infection and immunosuppressive drugs are most often implicated but corticosteroids are the most consistent cause of hyperinfection in those with previously unsuspected chronic strongyloidiasis.⁴ This is of particular relevance to the neurosurgical population, who frequently receive pre-operative and postoperative steroids to minimise cerebral oedema.

Diagnosis of strongyloidiasis requires identification of the strongyloides larvae through microscopic stool or duodenal fluid examination, although this is not a sensitive method and repeated sampling may be required. Strongyloides serology (antibody detection via ELISA) is useful in chronic infection but can be negative in hyperinfection.⁸ Treatment is usually with oral ivermectin or albendazole, although neither is licensed in the UK.⁹ Strongyloides hyperinfection has been successfully treated in patients with impaired gastrointestinal function by the parenteral administration of a veterinary formulation of ivermectin.^{10–12}

Only one other report of disseminated *S stercoralis* infection following neurosurgery was identified in the literature.¹³ Simpson *et al*¹³ present the case of a resident of southeastern USA, an area where strongyloides is endemic, who developed cutaneous, respiratory and gastrointestinal symptoms following the resection of a glioblastoma. The patients in both cases had received steroids following intracranial surgery, and eosinophilia was not present in either case at the time of presentation; this is typical of strongyloides hyperinfection.⁴

Learning points

- ▶ Strongyloides hyperinfection should be included in the differential diagnosis of the septic patient recently given steroids if the patient originates from, or has visited, an area where strongyloides is endemic.
- ▶ Eosinophilia is rare in the strongyloides hyperinfection syndrome.⁴
- ▶ Strongyloides infection should be excluded prior to immunosuppression in those at risk of chronic strongyloidiasis.¹⁴
- ▶ Empiric treatment for strongyloides may be considered in those at risk of chronic strongyloidiasis when urgent administration of immunosuppressive drugs is required.
- ▶ Early input from a tropical disease specialist is advocated.

Competing interests None.

Patient consent Obtained.

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