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Unusual presentation of more common disease/injury

H1N1 disseminated infection in a 3-month-old boy

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Summary

Earlier this year a new influenza virus emerged. In children, the clinical manifestations of H1N1 infection are similar to those reported during periods of seasonal influenza. We report on a 3-month-old boy with an upper respiratory tract infection who presented enteropathy, coagulopathy and encephalitis related to H1N1. The infection was confirmed in nasopharyngeal aspirate, stools and cerebrospinal fluid by real-time PCR. Treatment with oseltamivir was started.

BACKGROUND

Earlier this year, a new influenza virus emerged and posed new challenges to the medical community. In Portugal, the first case was reported on the 4 May 2010. Up to the 1 April 2010, 115 adults and 7 children under the age of 18 years died in Portugal. Of all these children, only one did not have a relevant medical history.[1]

The clinical features of patients with H1N1 virus infection are generally similar to those reported during peak periods of seasonal influenza and past pandemics.[2] We report a case of pandemic influenza A related disseminated infection with coagulopathy, enteropathy and encephalitis in an infant aged 3 months. This is a rare manifestation associated to H1N1.

CASE PRESENTATION

A 3-month-old boy was admitted to our paediatric intensive care unit with bloody diarrhoea and severe coagulopathy. He had been in good health until 1 week before admission when an upper respiratory airway infection started. He was seen by his family doctor and an acute otitis media was diagnosed. Four days before admission, he presented with several episodes of watery diarrhoea that during the next few days became bloody and with mucus. He never had fever, vomits, loss of appetite or alteration in consciousness.

He was a healthy black boy, born at 38 weeks of gestational age, exclusively breast fed, fully immunised with rotavirus and with a negative family history for diseases.

On initial examination he appeared acutely ill and was irritable. He was afebrile (35.7°C), with a blood pressure of 106/60 mm Hg, a heart rate of 157 bpm and a respiratory rate of 32 per min. Oxygen saturation measured by pulse oximetry was 98% on room air. His skin was pale, without petechial lesions, with a prolonged perfusion time. The mucous membranes were dry and the anterior fontanel was depressed. The abdominal examination revealed a palpable spleen and liver 3 cm below the costal margin. The remainder of the examination was normal.

After placing a peripheral line, he started bleeding from the venous puncture locations.

INVESTIGATIONS

The initial laboratory evaluation showed thrombocytosis and severe coagulopathy with prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT) (table 1). The blood gases, renal function and ionogram were normal. He was transferred to our paediatric intensive care unit.

A chest radiograph showed an interstitial infiltrate and the abdominal ultrasound was normal.

OUTCOME AND FOLLOW-UP

Normal saline fluid boluses, plasma, cryoprecipitate and vitamin K were administered at admission with progressive normalisation of coagulation parameters.

From the 2nd to the 11th day of admission he presented generalised oedema due to progressive hypoalbuminaemia and hypoproteinaemia. He had a minimum value of albumin of 1.2 g/dl and of total proteins of 3.2 g/dl. An amino acid based hypoallergenic infant formula was started.

On day 4, due to persistent irritability a lumbar tap was performed and the cerebrospinal fluid (CSF) revealed a total 25 cells/mm^3 with polymorphonuclear predominance, a protein level of 65.9 mg/dl and a glucose concentration of 82 mg/dl. Ceftriaxone (100 mg/kg/day) was prescribed.

Real time reverse-transcriptase PCR (CLART FluAvir Kit; Genomica S.A.U, Madrid, Spain) for H1N1 in nasopharyngeal, stool specimens and CSF were positive. Direct immunofluorescence for influenza A and B, adenovirus and syncytial respiratory virus in nasopharyngeal secretions were negative.

Specimens of blood were cultured and were sterile. The stool examination was negative for rotavirus and bacteria. The cultural examination and the PCR in CSF for adenovirus, enterovirus, cytomegalovirus and Epstein–Barr were negative. Serology for cytomegalovirus and Epstein–Barr was negative.

Oseltamivir (2 mg/kg, twice daily) was started on the 4th day of admission and prescribed for 5 days and ceftriaxone was stopped.

Table 1 Haematological analyses and C reactive protein (CRP) during the admission time

	Days of presentation			
	Admission	**Day 6**	**D12**	**D24**
Haematocrit (%)	28.6	20.4	19.3	27
Haemoglobin (g/dl)	9.6	7.3	6.8	9.3
Mean corpuscular volume (fl)	73.7	69.2	75.1	77.1
White cells (per ul)	21800	16500	27200	10500
Neutrophils (%)	54.9	65.6	55.0	17.8
Lymphocytes (%)	31.0	30.2	30.1	65.9
Eosinophils (%)	0.6	0.5	0.1	7.3
Monocytes (%)	13.4	3.6	14.7	8.0
Basophiles (%)	0.1	0.1	0.1	1.0
Platelets	912000	53000	16000	474000
Prothrombin time (s)	143	14.6	13.3	10.1
Partial thromboplastin time (s)	75.3	39.3	32.1	31.5
d-Dimer (ug/l)	50	179.5	125	92.8
Fibrinogen (mg/dl)	100	396	349	379
CRP (mg/dl)	0.79	5.79	9.6	0.24

Although he was clinically stable, he developed a progressive acute haemolytic anaemia with a haemoglobin value of 6.8 g/dl. The direct Coombs test was negative and the peripheral blood smear showed rare schizocytes, target cells and anisocytosis. He also had thrombocytopenia, discrete elevation of PT and aPTT with normal fibrinogen values. Transfusion of erythrocytes and platelets were necessary (table 1).

Due to the alterations in the central nervous system previous reported, an Upshaw-Schulman syndrome was suspected. The measurement of a disintegrin and metalloproteinase with a thrombospondin type 1 motif member 13 activity (ADAMST 13), the enzyme responsible for the degradation of the large multimers of Von-Willebrand factor, was normal.

The coagulation study revealed a decreased factor VII, antithrombin III and functional C protein. At discharge all these factors were rising. The complement activity was always unchanged.

The immunoglobulins and lymphocytic populations were studied and did not show alterations.

He was discharged with normal stools and blood analyses (table 1). After 1 month of follow-up all his blood tests had normalised and he had an appropriate psycho-motor development.

DISCUSSION

This case describes a severe and disseminated disease associated with the novel influenza A, swine-type H1N1 with involvement of the respiratory, gastrointestinal, haematological and central nervous system.

In children, seasonal influenza manifestations vary according to age, immunity status, medical conditions and previous contact with the virus. Among healthy children generally is an acute, self-limited and uncomplicated disease.[3] The classical manifestations of an upper respiratory tract infection are rare in infants under 2 years old in whom high grade fever, ill appearance and gastrointestinal symptoms are more likely to be present.

Acute otitis media and pneumonia are the most common complications associated to influenza.[4] Neurological complications like encephalitis, encephalopathy and aseptic meningitis have been described.[4 5] Morishima *et al*[6] reported 148 cases of encephalitis and encephalopathy associated with an influenza epidemic in Japan. In this study, 81.8% of the patients were under 5 years of age and the major clinical signs were loss of consciousness, convulsions, cough and vomiting.

According to the Centers for Disease Control and Prevention, people younger than 25 years of age are the most affected by this pandemic.[7] In the paediatric population, those with less than 12 months have the highest rates of hospital admissions and approximately 60% of children admitted to hospital have underlying medical conditions.[8]

Viral pneumonia, acute respiratory distress syndrome, secondary bacterial infection and exacerbation of airflow limitation have been reported as complications associated with swine influenza.[8]

Neurological disease caused by H1N1 was first notified on May 2009 in the USA.[9] Four children with influenza-like illness presented with seizures or altered mental status. The viral RNA was detected in nasopharyngeal specimens but not in the CSF.[9]

Although, in literature, there are some questions about the possibility that influenza virus do not directly invade the central nervous system, a few reports have obtained a positive PCR result in CSF for influenza type A.[10] This was the technique used by our laboratory to identify H1N1 in our patient.

With this case, the authors describe a very rare and severe presentation associated to this new influenza virus. Our patient had a disseminated infection with respiratory, gastrointestinal and neurological involvement and with a sepsis-like illness with an intravascular coagulation disorder. This late finding was evidenced by the microangiopathic anaemia, thrombocytopenia and coagulopathy with low levels of factor VII, antithrombin III and functional C protein that he developed.

In face of these blood alterations and mental status changes, an Upshaw-Schulman syndrome was suspected even though his renal function was normal. This disease was ruled out after a normal study of ADAMST 13 activity.

The negative results of PCR for adenovirus and enterovirus in CSF, of the ELISA for rotavirus and of viral serologies, blood and stool cultures, suggest that H1N1 was responsible for the haemorrhagic colitis, encephalitis and sepsis that the patient presented. The test used to diagnose H1N1 was named CLART FluAvir which has a 100% of sensitivity and specificity with a negative and positive predictive value of 100%.[11]

In this case, time from onset of illness to initiation of antiviral treatment was 1 week. Most studies suggest that the use of oseltamivir is beneficial in avoiding complications when started early in the course of the disease.[6] The small age of our child adding to the late prescription of oseltamivir were probably the factors that have most contributed to the severity of the clinical picture.

With this clinical report the authors want to draw attention to a serious and possible presentation of H1N1disease.

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Learning points

- Pandemic H1N1 has similar clinical manifestations to seasonal influenza.
- Complications associated to H1N1 can be severe.
- Disseminated infection is a possible complication that clinicians should be aware of.

Competing interests None.

Patient consent Obtained.

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