CASE REPORT

Transient acute adrenal insufficiency associated with adenovirus serotype 40 infection

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SUMMARY

We present an instance of a 6-year-old boy who was admitted with adenovirus infection and developed transient acute adrenal insufficiency, which required supplementation with glucocorticoids and mineralocorticoids for 8 weeks. Adenovirus has got adrenotropic potential and can cause adrenal insufficiency. We could not find any similar reported case in medical literature. We hope our case would add to the existing knowledge of adenoviral complications in paediatric patients.

BACKGROUND

Adenovirus is a common pathogen presenting with myriad forms of illnesses in the paediatric age group. Gastroenteritis and respiratory infections are most common among them. Adenovirus serotypes 40 and 41 are commonly identified in the gastroenteritis cases though others may also be seen. Transient suppression of adrenal function has never been reported.

CASE PRESENTATION

A 6-year-old male child was admitted in paediatric ward with a history of vomiting for the past 3 days. He had mild coryzal symptoms at the onset of illness. He had passed few soft stools in the past 24 h prior to admission. He was born at full term and had no relevant medical history. He was a thriving child with weight and height both plotting along 75th centiles. His energy levels prior to this presentation were good as reported by parents. He denied any sick contacts. At initial evaluation in the emergency department he was found to be moderately dehydrated and lethargic with blood glucose 4 mmol/L. He received one normal saline bolus and was admitted for intravenous rehydration.

After 48 h of admission he was still lethargic and his blood sugar dropped to 1.6 mmol/L at one occasion, which was replaced with bolus of 10% dextrose. His diarrhoea had stopped since admission but he continued to vomit intermittently and had developed very mild diffuse pain in central abdomen. Blood tests were ordered as his sluggishness was disproportionately more than what his vomiting would have accounted for. Blood tests revealed normal full blood counts with haemoglobin of 13.5 g/dL. Urea was 5.5 mmol/L; with creatinine 26 mmol/L; sodium 128 mmol/L; chloride 95 mmol/L and potassium 6 mmol/L. His liver function tests, calcium, phosphorus, magnesium, thyroid function tests and PTH (parathormone) levels were all normal. Urine output calculated over the past 24 h was 2.2 mL/kg/h. Next morning 08:00 cortisol and ACTH (adreno cortico trophic hormone) levels were 130 nmol/L (normal range 135–500 nmol/L) and 12 pmol/L, respectively. Short synachten test with 250 ng of intravenous ACTH did not show any rise in cortisol level after 60 min of administration. Low morning cortisol, high ACTH along with no response to short synachten test confirmed the clinical diagnosis of adrenal insufficiency. Plasma levels of VLCFA (very long chain fatty acids) mainly C24, C26 and their ratios were normal. His stool was positive for antigen of adenovirus. Blood PCR further confirmed adenovirus in blood and cell culture detected adenovirus serotype 40 from the plasma. Mantoux test was negative. Abdominal ultrasound, MRI of the brain and CT of the abdomen were reported normal. He was supplemented with oral hydrocortisone and fludrocortisone for the next 4 weeks. Repeat morning cortisol level after 4 weeks of presentation was 487 nmol/L and he subsequently underwent gradual withdrawl of both glucocorticoid and mineralocorticoid supplements. He was symptom free and off medication after 8 weeks of presentation with normal morning cortisol and ACTH levels.

OUTCOME AND FOLLOW-UP

He is doing well at 18 months follow-up.

DISCUSSION

Adenovirus infection is very common among children. Fox *et al*[1] reported in 1977 that it causes 5–10% of all fever among young children. Its various serotypes cause a wide variety of illnesses ranging from gastroenteritis to respiratory infections, keratoconjunctivitis, encephalitis and haemorrhagic cystitis. Myocarditis,[2] pancreatitis and disseminated infections have also been reported particularly in immunocompromised children.[3] Medvedev *et al*[4] demonstrated inflammatory changes in autopsied adrenal gland of 14 infants dying with generalised adenovirus and other viral infections. Adenovirus has got hepato and adrenotropic potential. It has been shown that adenovirus induces inflammatory cytokines as well as enhances the production of adrenal hormones as a host defense mechanism, after its administration as vectors in the human body.[5] In a recent study by Alesci *et al*[6] it has been reported that adenovirus can impair steroidogenesis in adrenal glands.

Owing to the fact that involvement of adrenal gland was transient in our patient, we support initial replacement of both glucocorticoid and

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mineralocorticoids for few weeks with regular monitoring of electrolyte and cortisol levels. Once levels become normal, the patient can be taken off medication. We acknowledge the lack of any evidence in this particular replacement therapy due to unavailability of natural history of adrenal involvement. Further studies and case reports are needed to substantiate this.

To our knowledge no case of adrenal insufficiency after wild adenovirus infection has been reported in medical literature. The above cited studies were performed either on clinically unproven autopsied sample or as a part of implicating adenovirus as an important vector for gene therapy in adrenal malignancies. It is quite interesting to see no such reports in spite of adenovirus being a common pathogen in the paediatric age group. One possible explanation might be not considering post illness lassitude and sluggishness as significant due to its eventual self-dissolution. Availability of blood tests to diagnose adrenal insufficiency at all the healthcare facilities is also a major limitation for physicians in performing the desired tests. The presence of subclinical adrenal suppression cannot be ruled out in lack of well-designed study showing postadenoviral adrenal status. Keeping in view how commonly adenovirus affects children, it is very important for clinicians to bear in mind its diverse consequences with hitherto unspoken, adrenal insufficiency in the list as well. Further researchers are invited to unveil adrenal insufficiency associated with adenovirus infection.

Learning points

- Adenovirus has got adrenotropic potential and can cause transient adrenal insufficiency.
- Clinical suspicion would help early diagnosis if a patient with resolving adenovirus infection presents with suggestive features.
- Adrenal hormonal supplementation may be required for the transient period.
- Further research is needed to consolidate the pathophysiology behind adrenal involvement of adenoviral infection.

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Competing interests None.

Patient consent Obtained.

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