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Acute Pancreatitis and Pancreatic Pseudocyst in a Toddler Following Mumps, Measles and Rubella Vaccine

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Abstract

Mumps, Measles and Rubella (MMR) vaccine has been marred by a lot of controversies since its inception. Acute pancreatitis is an uncommon condition in children and has been rarely reported following immunization. We report a toddler who developed acute pancreatitis and pancreatic pseudocyst following MMR vaccination. After ruling out other common causes, the chronology suggested the vaccine to be the possible etiology of pancreatitis. Though the exact mechanism of injury is not known, various possible mechanisms of vaccine related pancreatitis is postulated with autoimmunity being the most accepted. The report highlights a rare yet life-threatening complication following MMR vaccination which should alert the fellow Pediatricians as many of them may go un-noticed.

Keywords: Vaccine; Mumps-measles-rubella; Pancreatitis; Pseudocyst; Toddler

Introduction

Acute pancreatitis (AP), an uncommon condition in children, is predominantly secondary to pancreatico-billiary anomalies, drugs, infection, metabolic abnormalities and trauma. Rarely, it may give rise to pseudocyst formation [1]. Among the infectious etiologies of AP, viral agents, namely, Mumps, HIV (Human immune deficiency virus), Coxsackie B, Hepatitis B and Varicella zoster predominate [1]. Acute pancreatitis has also been sparingly reported after various viral vaccines, including Mumps [2], Mumps-Measles-Rubella (MMR) [3], Hepatitis A and B [4], Human papilloma virus (HPV) [5] and also after bacterial (Cholera and Typhoid) vaccines [6]. Though various theories are proposed, the actual mechanism of pancreatitis following vaccination has been unclear.

We report a toddler who developed acute pancreatitis and pancreatic pseudocyst after MMR vaccination. The case is being presented in view of its rarity and also to create awareness among fellow pediatricians who are expected to encounter this potential complication with widespread use of this vaccine.

Case Presentation

A-17-month old, premorbidly asymptomatic, appropriately immunized, healthy boy received first dose of Measles-Mumps and Rubella (MMR) vaccination as a part of his routine immunization schedule. He remained apparently asymptomatic for next 10 days when he developed acute onset abdominal distension, bilious vomiting, and irritability. There was no history of fever, rash, abdominal trauma, any drug intake, neck swelling, jaundice, decreased urine output or seizure. On examination, he was sick-looking with some dehydration. There was tachycardia, tachypnea, and generalized abdominal distension with diffuse tenderness. Investigations suggested mild microcytic, hypochromic anemia, neutrophillic leucocytosis, mildly increased transaminases with a normal renal function test and serum electrolytes. His serum amylase and lipase were markedly increased (Table 1) and ultrasound (USG) of abdomen revealed an enlarged, edematous pancreas with heterogenous echotexture and peripancreatic fluid collection, suggesting a diagnosis of acute pancreatitis. There were no apparent pancreatico-billiary anomalies, gall stones or pancreatic calculi. The child was managed conservatively with nil per oral, gastric decompression, intravenous fluid resuscitation and hydration, analgesia and intravenous antibiotics. Investigations for common causes of pancreatitis were non-contributory (Table 1). He recovered over next 7 days and could be discharged after 10 days. After 10 days of discharge, the child was again brought with a complaint of abdominal distension with a gradually increasing mass in the upper abdomen along with irritability and decreased feeding for 4 days.

Investigation	Result	Reference
Hemoglobin (gm/dl)	9.7	10-13.2
Total leucocyte count (/mm^3)	17500	4000-11000

Differential leucocyte count	Neutrophil 76%, Lymphocyte 19%, Monocyte 4%, Eosinophil 1%	Neutrophil 15-45%, Lymphocyte 47-77%, Monocyte 0-8%, Eosinophil 0-6%
Platelet count	2.9 lakh/mm^3	1.5-4 lakh/mm^3
Peripheral smear	Microcytic, hypochromic red blood cells with marked aniso-poikilocytosis	-
Sodium (mEq/L)	142	135-145
Potassium (mEq/L)	4.8	3.5-5
Urea (mg/dl)	33	Oct-34
Creatinine (mg/dl)	0.4	0.2-0.4
Random blood glucose (mg/dl)	86	8-180
Serum triglyceride (mg/dl)	86	<150
Total bilirubin/ conjugated (gm/dl)	0.5/0.1	<1.2/ <0.5
Total protein (gm/dl)	5.9	5.5-7.5
Albumin (gm/dl)	3.5	3.5-5.2
Serum glutamic-oxaloacetic transaminase (SGOT) (U/L)	66	13-45
Serum glutamic pyruvic transaminase (SGPT) (U/L)	83	13-45
Alkaline phosphatase (U/L)	312	150-420
Calcium (mg/dl)	8.9	09-Nov
Phosphate (mg/dl)	4.6	4-6.5
Amylase (U/L)	1524	<100
Lipase (U/L)	1112	<160
Blood culture	Negative	-
Hepatitis A IgM antibody	Negative	-
Hepatitis B surface antigen	Negative	-
HIV ELISA	Negative	-
Coxsackie virus B ELISA	Negative	-
Immunoglobulin G (mg/dl)	466	184-974
Antinuclear antibody (ANA)	Negative	-
Anti-islet cell antibodies	Negative	-
Sweat chloride estimation (mEq/L)	23	<40
d508 mutation of Cystic fibrosis transmembrane conductance regulator (CFTR) gene	Negative	-
Serine protease inhibitor Kazal-type 1 (SPINK 1) gene mutation	Negative	-

Table 1: Investigations of the patient.

There was no fever, vomiting, jaundice and he was passing urine and stool normally. Examination revealed stable vital parameters but the abdominal examination was remarkable with an ill-defined, palpable mass in the epigastric and left hypochondriac region which moved with respiration and had mild tenderness. There were no dilated veins or ascites. USG abdomen showed a large, thick walled cystic lesion in the region of the lesser sac, in close relation to greater curvature of stomach with thick internal echoes. Contrast enhanced computed tomography (CECT) scan of abdomen revealed the cystic lesion to be measuring approximately 8.7 cm × 10.3 cm × 11.2 cm,

compressing and displacing the stomach anteriorly. Posteriorly it compressed the pancreas with mildly prominent pancreatic duct (Figures 1 and 2). In presence of a persistently raised serum amylase of 766 IU/L, the features were suggestive of a pancreatic pseudocyst. In view of the large and increasing size of the pseudocyst, he underwent pseudocystogastrostomy with uneventful perioperative period. Currently 6 months into follow up, he remains asymptomatic.

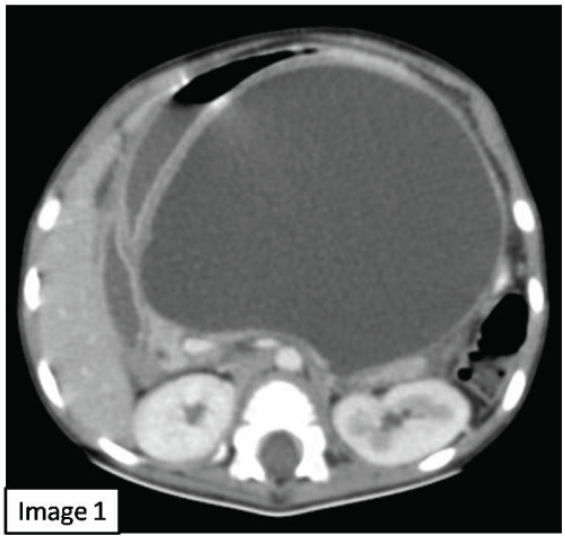

Figure 1: Axial contrast enhanced CT images of abdomen showing a large, thin walled, cystic lesion in the region of lesser sac with thinned out pancreatic parenchyma.

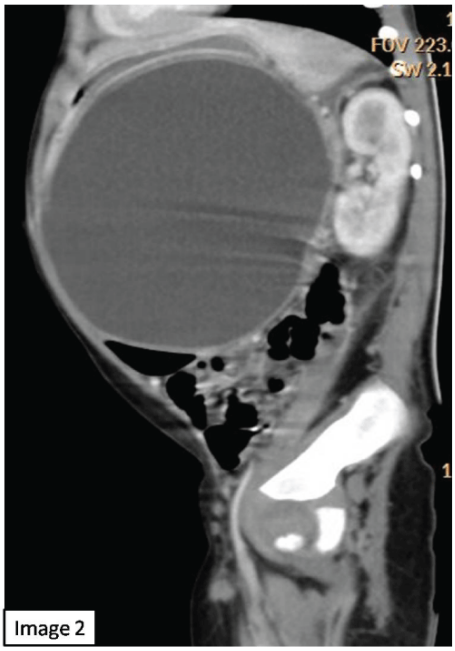

Figure 2: Sagittal contrast enhanced CT images of abdomen showing a large, thin walled, cystic lesion in the region of lesser sac with thinned out pancreatic parenchyma.

Discussion

Acute pancreatitis (AP) in the index child following MMR vaccination may be termed as 'probably' secondary to the vaccination as per the Adverse Events Following Immunization (AEFI) causality assessment criteria given by the World Health Organization (WHO) [7], as most of the common causes of AP in this age group was ruled out. The AP could be either a 'vaccine reaction' or purely 'coincidental' to the vaccination [7]. As suggested by Bijzak et al. [5] the following factors suggest a possible causal relationship of AP in this case with MMR vaccination:

- The chronology of events with the time period of clinical presentation corresponding to the incubation period of the Mumps virus.
- Previous reports of AP following MMR vaccine [3].
- Case reports of AP following other vaccines [2-4].
- Positive rechallenge and exacerbation of symptoms upon repeated exposure of the vaccine.
- Probable mechanism explaining the vaccine and AP.

The MMR vaccine, since its very inception, has been associated with many controversies relating to various adverse effects. A recent Cochrane database of systematic reviews [8] concluded that the vaccine is associated with aseptic meningitis, febrile seizure and possibly immune thrombocytopenic purpura but it did not seem to increase the risks of autism, asthma, leukemia, hay fever, type 1 diabetes, gait disturbance, Crohn's disease, demyelinating diseases, or bacterial or viral infections.

The previously used Mumps vaccine was also reported to be associated with AP, as 3 out of 104 Israeli soldiers were found to develop mild AP after vaccination [9]. Although the exact mechanism of vaccination related AP is unknown, numerous potential explanations have been proposed. Previous researchers believed it to be due to obstruction of the Ampulla of Vater by cytotoxic edema or secondary to direct invasion by the attenuated vaccine virus [3]. Currently, the Heterophilic reactivity or "molecular mimicry" theory has been most accepted. Vaccines have been shown to induce the production of autoantibodies in several animal models. In this theory, immunologic injury may be caused by (1) a cytotoxic antibody having a heterophilic reactivity to acinar cells; (2) polyclonal activation of lymphocytes; (3) "bystander activation" of self-reactive lymphocytes or (4) somatic mutation of immunoglobulin variable genes. Other possible mechanisms include pancreatic injury by vaccine-induced vasculitis or vaccine triggered release of mediators such as histamine and leukotrienes [4]. Further in support of the autoimmune hypothesis, various autoimmune phenomenon are described following use of adjuvant vaccines and has been termed as ASIA (Autoimmune/ Auto-inflammatory Syndrome Induced by Adjuvants) [10]; MMR also being an adjuvant vaccine may cause auto-immunity mediated pancreatic damage.

A re-challenge being impractical in the given scenario, the most plausible etiology of AP seems to be the preceding MMR vaccination. But one should always be cautious in attributing such a serious and potentially fatal adverse reaction to the vaccine as the fear of adverse side effects and concerns over vaccine safety has been found to be the major deterrent factor against vaccination in both general population and healthcare professionals [11].

The toddler in our case, despite being treated appropriately, developed pseudocyst of pancreas. There has been Mumps infection

related AP and pancreatic pseudocyst [12], but to the best of our knowledge there has been no reports of this rare complication of AP in a vaccine related case. Despite having a uncomplicated pseudocyst, our patient was managed surgically as he was symptomatic with a large cyst and expertise for endoscopic drainage was not available [13].

Conclusion

Pancreatitis is a rare yet potentially life-threatening adverse reaction following MMR vaccine, which fellow pediatricians need to be aware of. Given the difficulty in establishing the cause effect relationship coupled with the wide range of severity of AP, it may be under-reported in children following vaccinations. Therefore, the vaccine manufacturers should consider mentioning it as a potential complication of the vaccine.

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