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Case Report

Diabetic ketoacidosis in a child with congenital rubella syndrome: A case report and review of literature

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ABSTRACT

Congenital rubella syndrome (CRS) usually occurs in a developing fetus of a pregnant woman who has contracted rubella, usually in the first trimester. With universal rubella vaccination, the incidence of CRS in developed countries has drastically reduced. However, in developing countries, CRS continues to be a public health menace in children. Sensorineural deafness, cataract, micropthalamia, patent ductus arteriosus and pulmonary stenosis are common clinical manifestations in a child affected with CRS. Other relatively rare manifestations are hepatosplenomegaly, thrombocytopenia and blueberry muffin spots. Although it is well known that CRS predisposes towards development of diabetes mellitus usually in adults, but in children only anecdotal case reports are available. Latent viral infection, immune mediated mechanism and HLA allele predisposition are various possible pathogenic mechanisms. Majority of affected persons require insulin therapy. Hereby we are demonstrating a case of seven year old boy with CRS, who presented with diabetic ketoacidosis and was successfully managed with insulin therapy. This report intends to aware clinicians regarding predisposition of children with CRS for developing diabetes, as timely diagnosing and instituting insulin therapy will help in avoiding complications and improving their quality of life.

1. Introduction

Congenital rubella syndrome (CRS) usually occurs in a developing fetus of a pregnant woman who has contracted rubella, usually in the first trimester [1]. With the advent of rubella vaccination, the incidence of CRS drastically reduced in developed countries [2]. However, in developing countries like India, incidence of CRS is still high to constitute a significant public health problem [2]. Recently launched measles-rubella (MR) campaign intends to change this scenario by increasing universal immunization coverage [2]. The risk of the fetus getting infected with CRS is as high as 81% in first trimester maternal infection [3]. This reduces to 54% in second trimester maternal infection, and Infants are not generally affected if rubella is contracted during the third trimester, or 26–40 weeks after conception [3]. CRS was first reported by Norman McAlister Gregg of Australia in 1941 [4]. Classic triad of clinical features of CRS include sensorineural deafness (58%), eye abnormalitie such as retinopathy, cataract, glaucoma, microphthalmia (43%) and congenital heart disease like pulmonary artery stenosis and patent ductus arteriosus (50%) [5]. Other less common manifestations of CRS are hepatosplenomegaly, bone marrow suppression, thrombocytopenic purpura and blueberry muffin skin lesions (areas of extramedullary hematopoisis) [5].A considerable proportion of these children often have microcephaly, intellectual disability and these children should be followed up for development of autism, learning disabilities and schizophrenia in later life [5]. Type 1 or insulin dependent diabetes mellitus is one of the extremely rare manifestations of CRS which usually develops in adolescents or young adults in about 1% of CRS affected individuals [6]. There are only few anecdotal case reports of children with CRS with diabetes mellitus [6]. Hereby we are documenting one such case of diabetes mellitus in seven year old boy with CRS, who was managed with dietary modification and insulin injection.

2. Case summary

The index case is a seven year old boy with a diagnosed case of congenital rubella syndrome under regular follow up since infancy. The child was born by spontaneous vaginal delivery at term with birth weight of 2.1 kg only. During antenatal period the child had

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fever with maculopapular rash lasting for 3–4 days in second gestational month, at the time of which they did not seek any formal medical consultation. No other complications occurred during antenatal period. At 2 weeks of age, the child was brought with complaints of suck-rest-suck cycle during feeding, with excessive forehead sweating.

On clinical examination, the child was found to have microcephaly, tachycardia, continuous murmur in second left infraclavicular space and cataract in right eye. In view of the above clinical examination findings, congenital rubella syndrome was suspected and IgM Rubella in serum was found to be strongly positive, thereby confirming the diagnosis. Brainstem evoked audiometry showed bilateral moderate sensorineural hearing loss. Echocardiogram showed 8 mm patent ductus arteriosus (PDA) with left to right shunt. MRI brain showed patchy signal changes in bilateral cerebral white matter in T2 and FLAIR images, consistent with congenital rubella infection (Fig. 1). On follow up, the child had mild intellectual disability, using hearing aids and cataract was surgically corrected in infancy.

At seven years of age, the child presented with fever and pain abdomen for 3 days and fast breathing for one day. Respiratory, cardiovascular and per abdominal examination was within normal limits, except for fast breathing and signs of some dehydration. Random blood sugar was 459 mg/dl and arterial blood gas showed high anion gap metabolic acidosis (pH-7.153, HCO [3]-9 meq/dl), along with pseudohyponatremia. Ketostix examination in urine was strongly positive. On leading questioning, the parents revealed that for last one month the child was having polyurea and polydipsia, with weight loss.

With a working diagnosis of moderate diabetic ketoacidosis, the child was started on Ringer's lactate and regular insulin. Once the ketoacidosis resolved and blood sugar reached <200 mg/dl, the child was gradually shifted to intermittent subcutaneous injections with NPH and regular insulin. The parents were advised regarding dietary modification, subcutaneous injection technique, home blood sugar monitoring, correction factor for insulin injection in adjustment with blood sugar and sick day management. The child did not have any renal, neurological or retinal complications on screening. Lipid profile and thyroid function testing were also within normal limits. Currently on follow up at six months, the child is on daily intermittent subcutaneous insulin regimen, without any other clinically significant events.

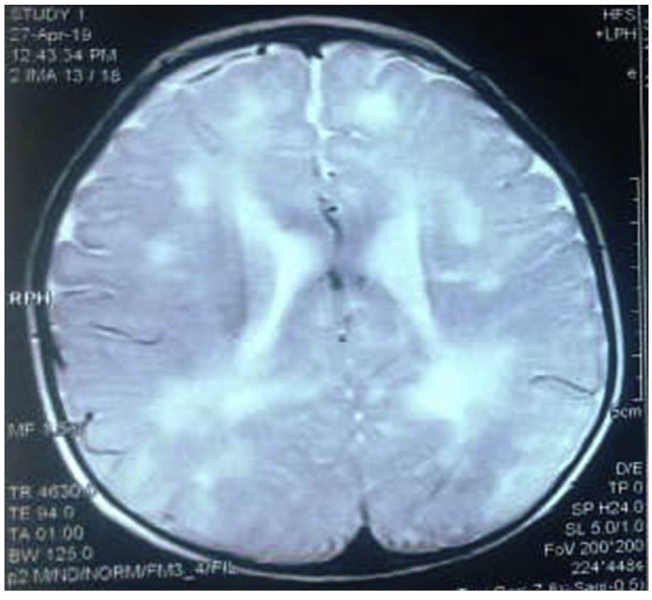

Fig. 1. Axial T2 weighed MRI brain of the child showing bilateral periventricular white matter signal changes consistent with congenital rubella syndrome.

3. Discussion

Diabetes in CRS was initially reported by Forrest et al., in 1969 and by Menser et al., in 1974. CRS is almost eliminated from developed countries due to universal rubella immunization in childhood [7,8]. Still congenital rubella infections has an interesting prospect of an immunological model for type 1 insulin dependent diabetes, as first proposed by Ginsberg-Fellner et al. [9]. The early reports grossly overestimated the prevalence of type 1 diabetes in children with congenital rubella syndrome even up to 20% [8]. However, a recent review was able to identify few anecdotal case reports and small case series only [9]. The review concluded that CRS undoubtedly predisposes to diabetes in later life, but the risk is low. This review also demonstrated that risk in childhood of developing diabetes from CRS is extremely low and more in those children who were severely underweight at birth [9].

Like the index case described above, previously all cases in childhood also presented with diabetic ketoacidosis at diagnosis, and were invariably treated with insulin [10]. Some adolescents and young adults presented also in much the same way. However, older age group people with CRS sometimes did not require insulin therapy and a subgroup indeed had insulin-resistant form of diabetes [10]. Many affected patients of CRS although do not satisfy the diagnostic criteria for diabetes mellitus, but definitely have impaired glucose tolerance [11]. Pathogenesis of diabetes in CRS has been attributed to various pathophysiological mechanisms [11]. One school of thought suggests direct infection of pancreatic beta cells by virus in early stage of life followed by reactivation of latent infection later. T cell and B cell mediated immune damage; antigen mimicry and HLA predisposition have also some possible role, as described by Gale et al. [12].

The main evidence for an immune-mediated type of diabetes came from a referral centre in New York by Rubinstein et al., which found that 15/272 children with the CRS required continuous insulin therapy, while one other used insulin intermittently, and 14 others had abnormal glucose tolerance [13]. They also demonstrated an excess of the type 1 susceptibility allele HLA-DR3 and an absence of the protective allele HLA-DR2 in those affected with diabetes [13]. The authors postulated that rubella infection had merely increased the penetrance of type 1 diabetes [13].

4. Conclusion

The clinicians treating children with congenital rubella syndrome should be aware of their predisposition for developing diabetes, as timely diagnosing and instituting insulin therapy will help in avoiding complications and improving their quality of life. There is need for large, multicentric longitudinal prospective clinical studies to determine exact incidence of diabetes mellitus in children with congenital rubella syndrome, its exact etiopathogenesis and risk factors determining its occurrence.

Conflicts of interest

Nil.

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Nil.

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