International Journal of Healthcare and Medical Sciences
ISSN(e): 2414-2999, ISSN(p): 2415-5233
Vol. 7, Issue. 3, pp: 26-30, 2021
URL: https://arpgweb.com/journal/journal/13
DOI: https://doi.org/10.32861/ijhms.73.26.30

Academic Research Publishing Group

A Report **Open Access**

Charge Syndrome Hallmarked with Wolff-Parkinson-White Syndrome and Patent Ductus Arteriosus; 20 Years Post-Repairing; An Extreme Combination

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Article History
Received: 9 April, 2021
Revised: 17 May, 2021
Accepted: 6 June, 2021
Published: 10 June, 2021

Abstract

Rationale: CHARGE syndrome or Hall-Hittner syndrome is a pleiotropic disorder, in which the name is derived from the abbreviation epitomizing its six clinical criteria: ocular coloboma, cardiac defects, choanal atresia, growth or developmental retardation, genital hypoplasia, and ear anomalies or deafness. Wolff-Parkinson-White syndrome is the most frequent pattern of ventricular pre-excitation. Patent ductus arteriosus is one of the most frequent congenital heart diseases due to failure of closure of the ductus arteriosus within 72 hours of birth. CHARGE syndrome, Wolff-Parkinson-White syndrome, and patent ductus arteriosus are so difficult to be present in a single entity. Patient concerns: A young female girl patient presented to the physician's outpatient clinic with acute confusion status with a past repaired patent ductus arteriosus. Diagnosis: CHARGE syndrome hallmarked with Wolff-Parkinson-White syndrome and patent ductus arteriosus; 20 years post-repairing. Interventions: Plain chest x-ray, electrocardiography, oxygenation, and echocardiography. Outcomes: A dramatic clinical improvement post-oxygenation had happened. Lessons: CHARGE syndrome with Wolff-Parkinson-White syndrome and repaired patent ductus arteriosus is an extreme combination. The existence of infantile electrocardiographic Tee-Pee sign of hypocalcemia and adult low ionized calcium with CHARGE syndrome is highly suggestive of associated DiGeorge phenotype syndrome. An absence of tachycardia post- repairing of patent ductus arteriosus from 11 mo until the 20th-year-old is a good prognostic sign. The presence of an infantile T-wave alternance will strengthen both the risk of serious arrhythmia and the efficacy of patent ductus arteriosus repairing.

Keywords: CHARGE syndrome; Hall-hittner syndrome; Wolff-parkinson-white syndrome; Patent ductus arteriosus; Genetic syndromes.

1. Introduction

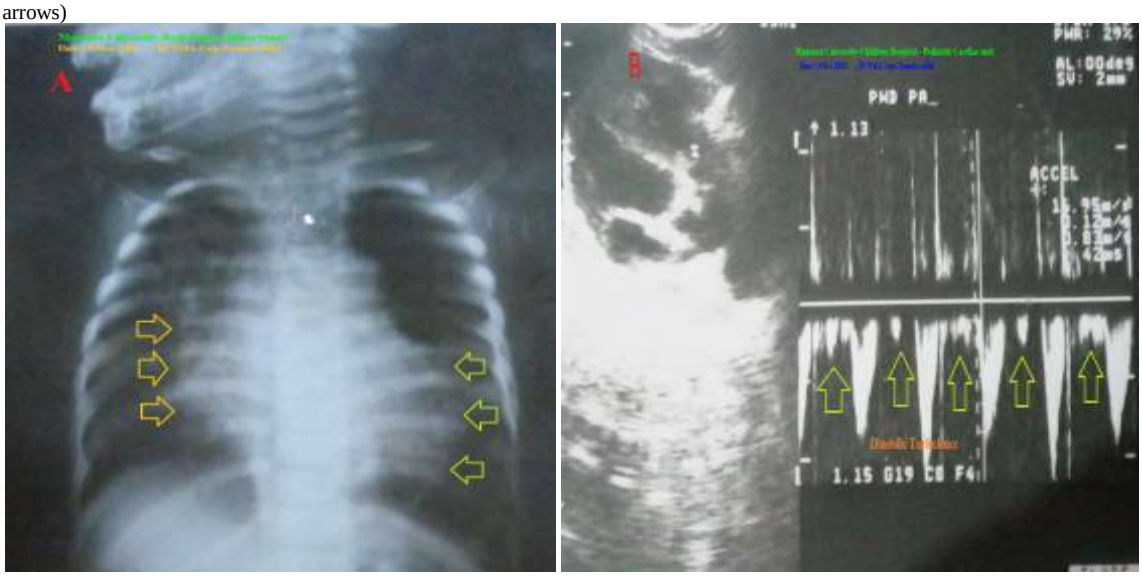
CHARGE syndrome or Hall-Hittner syndrome is a pleiotropic disorder, in which the name is derived from the abbreviation epitomizing its six clinical criteria: ocular coloboma, cardiac defects, choanal atresia, growth or developmental retardation, genital hypoplasia, and ear anomalies or deafness [1]. CHARGE syndrome was initially described as a non-random group of anomalies (Coloboma, Heart defect, Atresia choanae, Retarded growth and development, Genital hypoplasia, Ear anomalies/deafness). In 1998, an expert group had triaged both the major (the classical 4C's: Choanal atresia, Coloboma, Characteristic ears, and Cranial nerve anomalies) and minor criteria of CHARGE syndrome. Minor criteria including; cardiovascular malformations, pubertal delay, orofacial cleft, characteristic face, growth deficiencies, and developmental delay [2]. Patients who have all four major criteria or three major and three minor criteria are strongly likely to have CHARGE syndrome [2]. Nevertheless, CHARGE syndrome may be identified without the classical choanal atresia and coloboma. The announced incidence of CHARGE syndrome depends on current literature is ranges from 0.1–1.2/10,000 [2]. CHARGE syndrome is occasionally associated with DiGeorge phenotype[1]. DiGeorge anomaly is characterized by thymic agenesis, hypoparathyroidism, and heart and vascular anomalies [3]. **Wolff-Parkinson-White syndrome** (WPW) is the most frequent pattern of ventricular pre-excitation [4]. Wolff-Parkinson-White Syndrome is described as the existence of an accessory pathway (AP) that has a susceptibility to the emerging of supraventricular tachyarrhythmia. Conduction over an AP encircles conduction delay in the atrioventricular node (AVN), which causes unexpected eccentric stimulation of the ventricles and the formation of fusion complexes [5]. Wolff-Parkinson-White Syndrome diagnosed if there is symptomatic recurrent tachyarrhythmia with the following ECG criteria; 1. Shortened P-R interval of <0.12 s. 2. Slurred slow rising onset to QRS complex known as the delta-Wave and 3. A prolonged QRS complex >0.11 s [6]. Unstable patients with WPWS and AF should receive immediate electrical cardioversion. Stable patients can be chemically cardioverted with IV procainamide [5]. Immediate referral to cardiology is imperative for risk triage via electrophysiological study (EPS) [4]. Radiofrequency ablation is a choice therapy. This

is especially remarkable yielding that the long use safety of many antiarrhythmic medications has not been quietly clarified [4]. **Patent ductus arteriosus (PDA)** is one of the most frequent congenital heart diseases. A PDA, defined as failure of closure of the ductus arteriosus (DA) within 72 hours of birth [7]. Patent ductus arteriosus was initially identified at 1757 AM but it was given attentiveness as a congenital cardiac defect in the mid-nineteenth century [8]. A PDA is present in 40-60 % of preterms but its incidence is inversely proportional to the gestational age [9]. The DA assists as a considerable physiological communication in prenatal life. But the persistence of DA in postnatal life is undoubtedly a pathological anomaly due to its accompanied morbidity and mortality [8]. The patency of DA is mostly dependent on oxygen tension (PaO2) and prostaglandins (PGs) circulating levels [8]. Symptoms of PDA are relevant to the size of the DA and the degree of left-to-right shunting. Infants who present with small PDA may have minimal or no symptoms. But who present with large PDA will increases the susceptibility of risk for evolution to pulmonary hypertension [10]. Indomethacin is a PG inhibitor that has been used for the closure of PDA since the late 1970s [11]. The surgical used methods for the closure of PDA comprise using coils, vascular clips and, suture ligation by traditional intercostal incision or by video-assisted thoracoscopic approach [8].

2. Case Presentation

A 20-year-old single, student, young, Egyptian female patient presented to the physician outpatient clinic (POC) with acute confusion state. No more associated symptoms. Her mother gave a history of patent ductus arteriosus since 3 mo after developing acute respiratory distress syndrome and severe pulmonary hypertension (Figure 1A and 1B) and repaired on 11 mo. The patient had a simultaneous history of tachycardia (of VR; 160 bpm) with WPW syndrome only before repairing of patent ductus arteriosus (Figure 1C). With increasing age, the mother had started to notice the difficulty of learning, intellectual defects, blurred vision, diminished hearing, intermittent mucus nasal discharge, intermittent nasal obstruction, growth retardation, amenorrhea, and hypogonadism. Otherwise tachycardia, the mother frequently had consulted the specialists for the above complaints. Informed consent was taken from her father. Currently, upon general physical examination; generally, the patient seemed mentally retarded, infantile facies, small eyes, deaf, glassy blurred vision with iris defects (Figure 2). Pulse rate was regular at VR; 68 bpm, blood pressure (BP) of 110/70 mmHg, respiratory rate of 16 bpm, the temperature of 36.8 °C, and pulse oximeter of oxygen (O2) saturation of 98%. No more relevant clinical data were noted during the clinical examination The current The current complete blood count (CBC); Hb was 11.9 g/dl, RBCs; $5.15*10^3/mm^3$, WBCs; $9.7*10^3/mm^3$ (Neutrophils; 63.3 %, Lymphocytes: 28.4%, Monocytes; 7.6%, Eosinophils; 0.5% and Basophils 0.2%), MCV was low (77.3 fl), MCH was low (23.1 pg), MCHC was low (29.9 g/dl), Platelets; $406*10^3/mm^3$. S. Ferritin was low (8.13 ng/ml). D-dimer was normal (100 ng/ml). CRP was normal (less than 1 g/dl). SGPT was normal; 18 U/L, SGOT was normal; 33 U/L. Both Serum creatinine showed (0.7 mg/dl) and blood urea (25 mg/dl) was normal. RBS was normal (84 mg/dl). Ionized calcium was mildly low; 0.83 mmol/L. The troponin test had become negative. The present plain chest x-ray film was nearly taken after 20 years after PDA closure showing no abnormalities (Figure 3A) and echocardiography was taken after 20 years after PDA closure showing no abnormalities (Figure 3B). ECG tracing was nearly taken after 20 years after PDA closure showing WPW syndrome of VR of 67 with delta waves, wide-QRS complex, and short P-R interval. There is no T-wave alternance. P and delta waves are upright in V1 (Figure 3C). CHARGE syndrome hallmarked with Wolff-Parkinson-White syndromes and patent ductus arteriosus; 20 years post-repairing was **the most probable diagnosis**. The patient was only treated with O2 inhalation by O2 cylinder (100%, by nasal cannula, 5L/min). A dramatic clinical improvement post-oxygenation had happened. Oral calcium, vitamin-D preparation, and iron supplements for 30 days were prescribed with further recommended cardiac and endocrinologist follow-up.

Figure-1. A-Plain Chest X-Ray film was taken on the 5th mo of life showing enlargement of RV (lime arrows) and RA (golden arrows). **B-Echo Doppler image** was taken on the 3rd mo of life showing diastolic turbulence. **C-ECG** was taken on the 3rd mo of life showing WPW syndrome with delta waves (red arrows), wide QRS (purple rectangle), and short P-R interval (green rectangle). There is a T-wave alternance in V2,4,5, and V6 (lime and golden arrows). There is also a Tee-Pee sign of hypocalcemia (green arrows). P- and delta waves are inverted in V1 ((blue arrows)



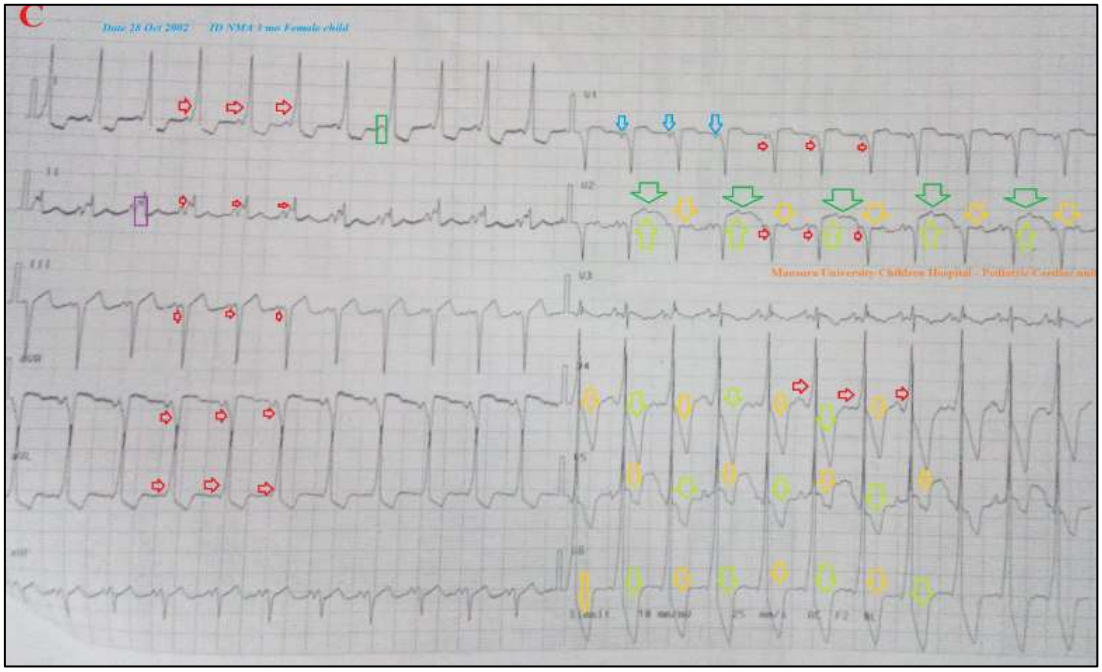


Figure-2. Patient face showing coloboma (lime arrows) microphthalmia (purple arrows) and bilateral choanal atresia (light blue arrows)

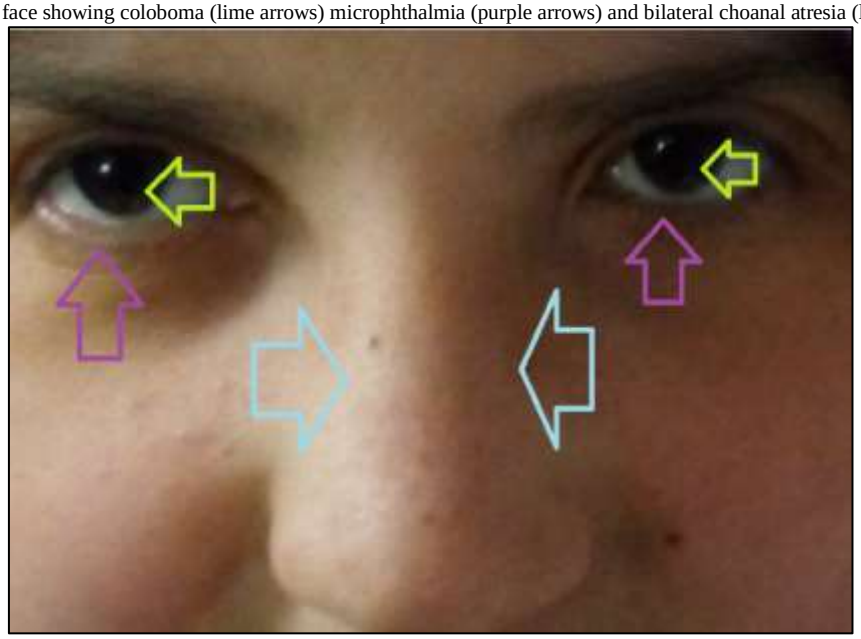
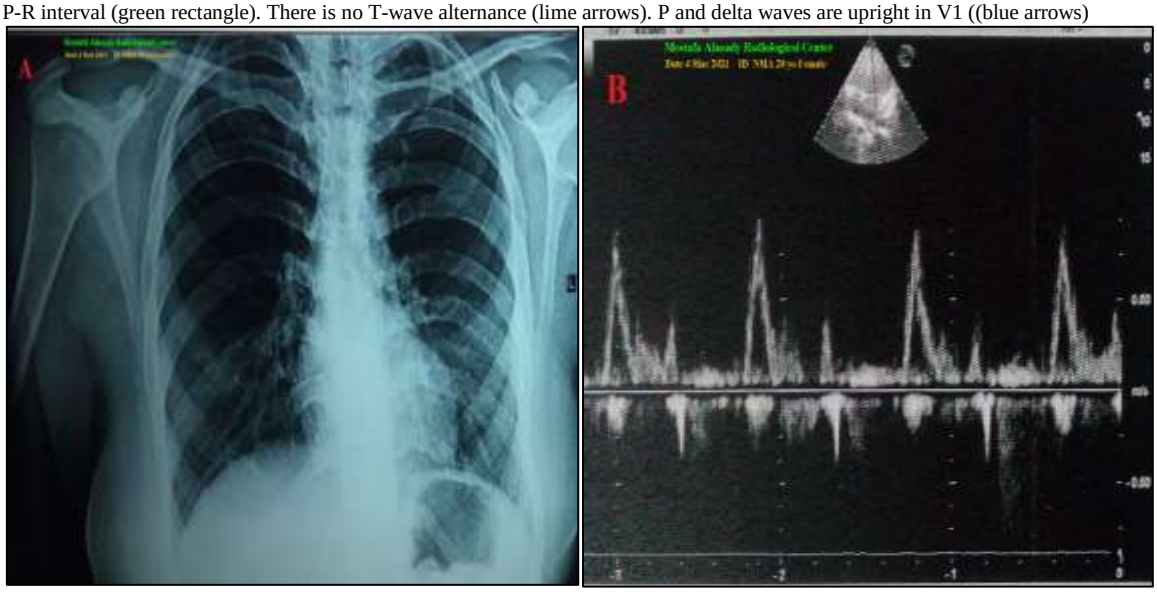
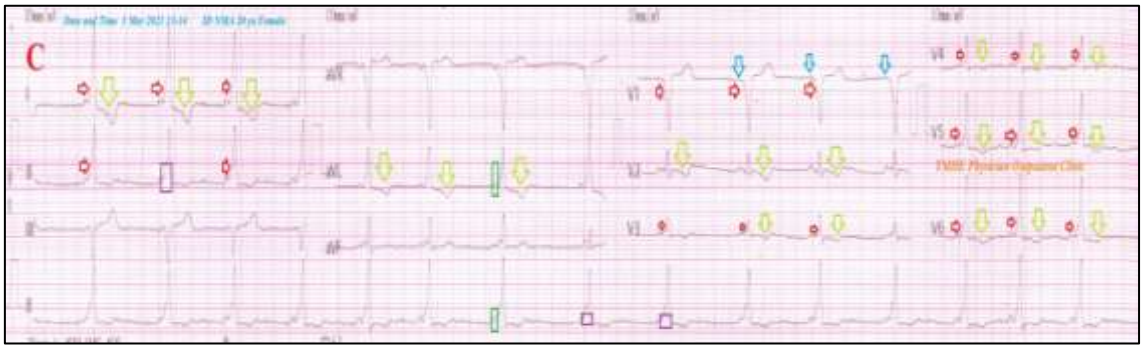


Figure-3. Plain chest x-ray film (A) and Echo-Doppler image (B) was taken after 20 years after PDA closure showing no abnormality. ECG tracing (C) was taken after 20 years after PDA closure showing WPW syndrome with delta waves (red arrows), wide QRS (purple rectangle), and short P-R interval (green rectangle). There is no T-wave alternance (lime arrows). P and delta waves are upright in V1 ((blue arrows)





3. Discussion

- **Overview:** A young female girl patient presented to physician outpatient clinic with acute confusion status with a past repaired patent ductus arteriosus.
- **The objective primary** for my case study was the presence of CHARGE syndrome with electrocardiographic Wolff-Parkinson-White syndrome and repaired patent ductus arteriosus.
- **The secondary objective** for my case study was the question of; How did you manage the case?
- The presence of coloboma (microphthalmia with blurred vision), heart defects (PDA), atresia of the choanae (intermittent nasal obstruction and mucus nasal discharge), retardation (of growth, intellectual, and learning), genital defects (hypogonadism, amenorrhea), and ear anomalies (diminished hearing).
- The presence of infantile T-wave alternance ay be reflect efficacy of PDA repairing.
- The existence of infantile electrocardiographic Tee-Pee sign of hypocalcemia and adult low ionized calcium in charge is an interesting
- Suspected iron deficiency anemia may interpret the acute confusion status which was dramatically responded to O2 inhalation.
- I can't **compare** the current case with similar conditions. There are no similar or known cases with the same management for near comparison.
- The only **limitation of the current study** was the unavailability of genetic counseling and diagnostic test.

4. Conclusion and Recommendations

- CHARGE syndrome with Wolff-Parkinson-White syndrome and repaired patent ductus arteriosus is an extreme combination**.**
- The existence of infantile electrocardiographic Tee-Pee sign of hypocalcemia and adult low ionized calcium with CHARGE syndrome is highly suggestive of associated DiGeorge phenotype syndrome.
- An absence of tachycardia post- repairing of PDA from 11 mo until the 20th-year-old is a good prognostic sign.
- The presence of an infantile T-wave alternance will strengthen both the risk of serious arrhythmia and the efficacy of patent ductus arteriosus repairing.

Conflicts of interest

There are no conflicts of interest.

Acknowledgment

I wish to thanks my wife to save time and improving the conditions for helping me.

Abbreviations

AP: Accessory pathway
CBC: Complete blood count
CHARGE syndrome: Coloboma, Heart defect, Atresia choanae, Retarded growth and development, Genital hypoplasia, Ear anomalies/deafness
DA: Ductus arteriosus
ECG: Electrocardiography
O2: Oxygen
PDA: Patent ductus arteriosus
POC: Physician outpatient clinic
SGOT: Serum glutamic-oxaloacetic transaminase
SGPT: Serum glutamic-pyruvic transaminase
VR: Ventricular rate
WPW syndrome: Wolff-Parkinson-White syndrome

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