CASE REPORTS

Acceleration of the ventricular response to atrial flutter by amiodarone in an infant with Wolff-Parkinson-White syndrome

J A Till, Mark Baxendall, A Benetar

Abstract

Amiodarone resulted in a rapid ventricular response to atrial flutter in an infant with Wolff-Parkinson-White syndrome.

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In a patient with Wolff-Parkinson-White syndrome the ventricular response to an atrial arrhythmia is determined both by the atrioventricular node and the accessory connection. There is a small risk of sudden death in the Wolff-Parkinson-White syndrome that is thought to result from ventricular fibrillation arising from a rapid ventricular response to an atrial arrhythmia through the accessory connection.^{1,2} Digoxin and verapamil may increase the risk of ventricular fibrillation in certain patients and are therefore usually avoided in the management of patients with Wolff-Parkinson-White syndrome.³ We describe an infant with Wolff-Parkinson-White syndrome in whom amiodarone resulted in a rapid ventricular response to atrial flutter.

Case report

A male infant was born to a 26 year old white mother. Pregnancy was uncomplicated until 29 weeks' gestation when an irregular fetal heart rhythm was noted. A fetal echocardiogram showed a structurally normal heart with an irregular rhythm diagnosed as atrial extrasystoles, but no other abnormalities were identified. A repeat scan performed at 32 weeks again confirmed an irregular fetal cardiac rhythm but no evidence of sustained tachycardia or fetal hydrops. Spontaneous labour started at 37 weeks' gestation and on admission of the mother to the labour ward the fetal heart rate was noted to be high and sustained. An emergency caesarean section was therefore performed and a grossly hydropic live infant was delivered. The infant was bradycardic with a low cardiac output and immediate resuscitation was required with intubation, ventilation, and external cardiac massage. The infant's condition was stabilised and transfer to a cardiac unit arranged. An echocardiogram confirmed a structurally normal heart but with considerable dilatation of the right atrium and ventricle with poor systolic function. There were bilateral pleural effusions, a small pericardial effusion, and ascites and the infant required

ventilation in 100% oxygen. During the first 24 hours of life there were two episodes of supraventricular tachycardia with further clinical deterioration. A 12 lead electrocardiogram during tachycardia showed a regular narrow QRS complex consistent with atrioventricular reentry tachycardia. Preexcitation was evident on an electrocardiogram recorded during sinus rhythm (fig 1A). The initial attacks of supraventricular tachycardia responded to vagal manoeuvres. None the less intravenous amiodarone was started at a dose of 5 mg/kg. Immediately after amiodarone treatment was started the child sustained a severe cardiovascular collapse with a wide complex bradycardia that required isoprenaline and further resuscitation. This restored supraventricular tachycardia which seemed to respond to direct current cardioversion but on later inspection the electrocardiogram showed atrial flutter with 2:1 atrioventricular nodal block (fig 1B). The infant's haemodynamic condition again stabilised but during the next 24 hours he became anuric and peritoneal dialysis was started. Regular oral amiodarone was given at a dose of 350 mg/m²/day (loading dose) and the infant remained stable over the following 10 days. Renal function recovered and after seven days the amiodarone concentration was 1 µg/l. However, after 10 days of amiodarone treatment a rapid wide complex tachycardia developed (fig 2). This was interpreted as preexcited atrial flutter. The atrial flutter rate had slowed and was conducted in a 1:1 fashion. Amiodarone was stopped and an elective cardioversion was performed, restoring sinus rhythm. The infant slowly recovered and oral propranolol was introduced. No further attacks of supraventricular tachycardia have been noted.

Discussion

When atrial flutter and atrial fibrillation occur in the Wolff-Parkinson-White syndrome a rapid ventricular response to such an atrial arrhythmia has been associated with haemodynamic collapse and sudden death.^{1,2} The ventricular response to an atrial arrhythmia is determined by several factors including the characteristics of both the accessory connection and the atrioventricular node, the atrial and ventricular refractory periods, and the degree of adrenergic stimulation.⁷ Assessment

Department of
Paediatrics, National
Heart and Lung
Institute, London
J A Till

Department of
Paediatrics, Royal
Postgraduate Medical
School, Hammersmith
Hospital, London
M Baxendall
A Benetar

Correspondence to:
Dr J A Till,
Department of Pacing and
Electrophysiology, Royal
Brompton, National Heart
and Lung Hospital, Sydney
Street, London SW3 6NP.

Figure 1 (A) Electrocardiogram from leads V1, II, and V5 showing overt preexcitation during sinus rhythm. (B) Leads V1, II and V5, during atrial flutter with 2:1 atrioventricular block. The atrial rate is 375 beats per minute. Paper speed 25 mm/s.

of the anterograde effective refractory period of the accessory connection has been suggested to be of value in predicting those patients at risk. This value correlates well with the

mean or minimum RR interval seen in either induced or spontaneously occurring atrial fibrillation.⁷ Drugs such as digoxin and verapamil can

Figure 2 A 12 lead electrocardiogram showing preexcited atrial flutter with a ventricular rate of 210 beats per minute. Paper speed 25 mm/s.

have an adverse effect in the presence of an atrial arrhythmia in that the ventricular response may quicken. In a patient with Wolff-Parkinson-White syndrome intravenous verapamil or digoxin can cause such a rapid ventricular response that ventricular fibrillation follows.³⁻⁶ Sudden death after oral administration of digoxin or verapamil in patients with Wolff-Parkinson-White syndrome is well recognised.⁴⁻⁶ The predominant effect of the drugs has been suggested to be a direct action on the accessory connection causing a shortening of the anterograde effective refractory period. Other mechanisms may play a part in that both drugs have a profound effect on atrioventricular nodal conduction and slowing of atrioventricular nodal conduction may restrict the number of impulses reaching the ventricular end of the accessory connection in patients who would normally conduct atrial fibrillatory impulses in part by their atrioventricular node and in part by their accessory connection. The number of impulses limiting anterograde conduction would therefore be less. In addition, the peripheral vasodilatation that follows verapamil treatment may cause a reflex increase in adrenergic tone, which in turn may further shorten the anterograde refractory period of the accessory connection or make the ventricular myocytes more susceptible to fibrillation.

Antiarrhythmic drugs which lengthen the anterograde effective refractory period have been suggested to be of value in the treatment of patients with Wolff-Parkinson-White syndrome who have had or who are judged to be at risk of ventricular fibrillation. Such drugs include the class 1 agents disopyramide, flecainide, and propafenone and amiodarone.⁸⁻¹⁰ In trials to assess the effect of drugs on an accessory connection amiodarone was the most consistent in lengthening the anterograde effective refractory period.¹¹ Such an effect was greatest in those patients with accessory connections with a long refractory period—that is, longer than 270 ms. Most drugs achieved only minimal effects in those patients with very short refractory periods. However, of all the drugs tested amiodarone was the most effective in those patients with a refractory period less than 270 ms.

Several mechanisms may have contributed to the onset of preexcited atrial flutter in the infant we report. The major electrophysiological actions of amiodarone are to increase the refractory period of atrial and ventricular tissue and slow conduction in the His-Purkinje system. In our case amiodarone slowed the flutter rate and in doing so allowed conduction in a 1:1 fashion through the accessory connection where it had not been possible at the higher rate. Restriction of atrial impulses reaching the ventricular end of the accessory connection through the atrioventricular node because of His-Purkinje slowing may have contributed by further limiting any concealed entrance to the ventricular end of the accessory connection. The direct effect of amiodarone on the effective refractory period of the accessory connection cannot be assessed.

Atrioventricular reentry tachycardia is the commonest supraventricular tachycardia encountered in the newborn infant and can result in cardiovascular collapse or death in this age group.¹² Management of an arrhythmia in the newborn hydropic infant with poor ventricular function is difficult. Such management problems are aggravated if the infant is preterm, and it has therefore been recommended that a trial of inutero therapy for a fetal arrhythmia may be better than early delivery.^{13,14} Unfortunately in our patient sustained supraventricular tachycardia was not detected by two antenatal scans. An irregular fetal heart rhythm due to atrial or ventricular extrasystoles is common and is generally dismissed as a benign finding unconnected with structural abnormality.¹⁷ Allan stated that though some have suggested that an irregular rhythm may precede a tachyarrhythmia, this was not the case in her series of nearly 100 cases.¹⁵ An irregular rhythm from such a cause usually disappears spontaneously towards term or soon after birth.¹⁵⁻¹⁷ Hydrops was not detected in this infant despite a repeat scan, and spontaneous onset of labour at 37 weeks led to the delivery of an infant in poor condition.

The use of digoxin in this age group is controversial. Some physicians continue to use digoxin in the presence of preexcitation because the incidence of atrial fibrillation in infancy is rare. In a study by Deal *et al* four of the 85 children presenting with supraventricular tachycardia before 4 months of age died over a mean period of 6.5 years.¹⁸ All four children were taking digoxin. Two had structural congenital heart disease in addition to Wolff-Parkinson-White syndrome but two died after a sudden cardiac arrest. Because digoxin can cause ventricular fibrillation in the presence of preexcitation even in small children we avoided digoxin in this infant and instead chose amiodarone. A class 1 drug or propranolol was not used because of the very poor contractile function of the heart. In addition the hepatobiliary mode of excretion of amiodarone was thought to be an advantage in this sick infant with acute tubular necrosis. The subsequent development of preexcited atrial flutter with an increase in ventricular response was not predicted. Such an increase in ventricular response to an atrial arrhythmia in a patient with Wolff-Parkinson-White syndrome as a result of amiodarone has been reported in an adult.¹⁹ In this patient, as with our case, the arrhythmia was promptly recognised and treated appropriately. Such a response is likely to be unusual but it is important that physicians treating such patients are aware of its occurrence.

There are two interesting aspects of this case; the first is the unusual but potentially life-threatening complication of amiodarone in the Wolff-Parkinson-White syndrome; the second is the development of near fatal fetal hydrops as a result of supraventricular tachycardia in a fetus previously scanned but untreated because atrial extra systoles were perceived as benign.

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