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Andhra Hospitals

The peoples pulse

E journal of Paediatrics

Issue. 1

Vol 2

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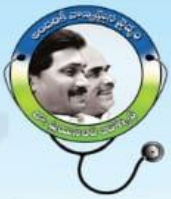

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Foreword

Greetings from the Andhra Hospitals!

For the past two decades, we are delivering excellence in terms of quality health care in the field of Paediatrics including Paediatric and Neonatal intensive care, Paediatric cardiac intensive care and other allied Paediatric sub-specialities.We take pride in introducing ECMO in pediatric specialty for the first time in the state of Andhra Pradesh. In this context, we convey our heartfelt thanks to you for your continued support and encouragement which played a pivotal role in our success.

As a token of our commitment to contribute to continuous medical education, we are introducing this monthly E-journal to showcase important clinical guidelines, recent advances in paediatric sub-specialties, interesting case reports, image quiz, OSCE scenarios etc, gathered from our patient database. We hope this endeavor would prove to be useful to practicing paediatricians, intensivists, neonatologists and post-graduate students.

Please send your valuable feedback and suggestions to ***maramkp@gmail.com*****.**

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PAEDIATRIC HYPERTENSION: AN UPDATE

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INTRODUCTION:

The development of a national database on normative blood pressure levels throughout childhood has contributed to the recognition of elevated blood pressure in children and adolescents. The epidemic of childhood obesity, the risk of developing left ventricular hypertrophy, and evidence of the early development of atherosclerosis in children would make the detection of and intervention in childhood hypertension important to reduce long-term health risks; however, supporting data are lacking. Secondary hypertension is more common in preadolescent children, with most cases caused by renal disease. Primary or essential hypertension is more common in adolescents and has multiple risk factors, including obesity and a family history of hypertension. Evaluation involves a thorough history and physical examination, laboratory tests, and specialized studies. Management is multifaceted. Non-pharmacologic treatments include weight reduction, exercise, and dietary modifications. Recommendations for pharmacologic treatment are based on symptomatic hypertension, evidence of end-organ damage, stage 2 hypertension, stage 1 hypertension unresponsive to lifestyle modifications, and hypertension with diabetes mellitus.

The prevalence and rate of diagnosis of hypertension in children and adolescents appear to be increasing. This is due in part to the increasing prevalence of childhood obesity as well as growing awareness of this disease. There is evidence that childhood hypertension can lead to adult hypertension. Hypertension is a known risk factor for coronary artery disease (CAD) in adults, and the presence of childhood hypertension may contribute to the early development of CAD. Reports show that early development of atherosclerosis does exist in children and young adults and may be associated with childhood hypertension. Left ventricular hypertrophy (LVH) is the most prominent clinical evidence of end organ damage in childhood hypertension. Data show that LVH can be seen in as many as 41 percent of patients with childhood hypertension. Patients with severe cases of childhood hypertension are also at increased risk of developing hypertensive encephalopathy, seizures, cerebrovascular accidents, and congestive heart failure. Based on these observations, early detection of and intervention in children with hypertension are potentially beneficial in preventing long term complications of hypertension. Data associating childhood hypertension with cardiovascular risk in adulthood are lacking. An update of recommendations for diagnosis, evaluation, and treatment of childhood hypertension is provided in the fourth report by the

National High Blood Pressure Education Program (NHBPEP) Working Group on High Blood Pressure in Children and Adolescents.

EPIDEMIOLOGY:

Because body size is an essential determinant of blood pressure in children, it is necessary to include the child's height percentile to determine if blood pressure is normal. The revised childhood blood pressure tables include 50th, 90th, 95th, and 99th percentiles by sex, age, and height based on the 1999- 2000 National Health and Nutrition Examination Survey data. Table 1 shows the classifications of hypertension for children one year of age or older and adolescents and the corresponding systolic and diastolic blood pressures. Blood pressure should be measured on three or more separate occasions before characterizing the type of hypertension. Reports have shown an association between blood pressure and body mass index (BMI) suggesting that obesity is a strong risk factor for developing childhood hypertension. There are insufficient data that define the role of race and ethnicity in childhood hypertension, although results of several studies show black children having higher blood pressure than white children. Heritability of childhood hypertension is estimated at 50 percent. One report noted that 49 percent of patients with primary childhood hypertension had a relative with primary hypertension, and that 46 percent of patients with secondary childhood hypertension had a relative with secondary hypertension. Another report showed that in adolescents with primary hypertension there is an overall 86 percent positive family history of hypertension. There is evidence that shows breastfeeding in infancy may be associated with a lower blood pressure in childhood.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation
Blood pressure should be checked routinely at every visit in children three years of age and older.
Three separate readings of an elevated blood pressure (greater than 90th percentile for age, height, and sex) on separate visits are needed to make the diagnosis of hypertension.
Patients diagnosed with primary hypertension should have a comprehensive assessment for cardiovascular risk factors (lipid profile, fasting glucose, body mass index).
Nonpharmacologic treatment (e.g., weight loss, dietary modifications, exercise) should be first-line therapy in patients with stage 1 hypertension.
Pharmacologic treatment should be initiated in patients with stage 2 hypertension, symptomatic hypertension, when end-organ damage is present (left ventricular hypertrophy, retinopathy, proteinuria); and in stage 1 hypertension when blood pressure is unresponsive to lifestyle changes.

TABLE 1

Classifications of Hypertension in Children One Year of Age and Older and Adolescents

Normal blood pressure	SBP and DBP less than the 90th percentile
Prehypertension	SBP or DBP greater than or equal to 90th percentile but less than 95th percentile Blood pressure levels greater than or equal to 120/80 mm Hg for adolescents
Hypertension	SBP or DBP greater than or equal to 95th percentile
Stage 1 hypertension	SBP or DBP from 95th percentile to 99th percentile plus 5 mm Hg
Stage 2 hypertension	SBP or DBP greater than 99th percentile plus 5 mm Hg

NOTE: *Percentiles are for sex, age, and height for blood pressure measured on at least three separate occasions; if systolic and diastolic percentiles are different, categorize by the higher value.*

SBP = systolic blood pressure; DBP = diastolic blood pressure.

BLOOD PRESSURE MEASUREMENT:

According to the NHBPEP recommendations, children three years of age or older should have their blood pressure measured when seen at a medical facility; however, according to the U.S. Preventive Service Task Force (USPSTF), there is insufficient evidence to recommend for or against routine screening for childhood hypertension to reduce the risk of CAD. The preferred method for blood pressure measurement is auscultation. Aneroid manometers are used to measure blood pressure in children and are accurate when calibrated on a semiannual basis. Correct measurement of blood pressure in children requires use of a cuff that is appropriate to the size of the child's upper right arm. This is the preferred arm because of the possibility of decreased pressures in the left arm caused by coarctation of the aorta. By convention, an appropriate cuff size is one with an inflatable bladder width that is at least 40 percent of the arm circumference at a point midway between the olecranon and the acromion (Figure 1). The cuff bladder length should cover 80 to 100 percent of the circumference of the arm (Figure 2). An oversized cuff can underestimate the blood pressure, whereas an undersized cuff can overestimate the measurement. Blood pressure should be measured in a controlled environment after five minutes of rest in the seated position with the right arm supported at heart level. If the blood pressure is greater than the 90th percentile, the blood pressure should be repeated twice at the same office visit to test the validity of the reading. Ambulatory blood pressure monitoring (ABPM) requires a patient to wear a portable monitor that records blood pressure over a specified period. This allows measurements outside of the medical setting, where some patients may experience elevated blood pressure caused by anxiety ("white-coat hypertension"). Other uses for ABPM include episodic hypertension, autonomic dysfunction, and chronic kidney disease.

ABPM also may have a role in differentiating primary from secondary hypertension and in identifying patients likely to have hypertension-induced end-organ damage.The USPSTF maintains that ABPM is subject to many of the same errors seen in the physician's office.

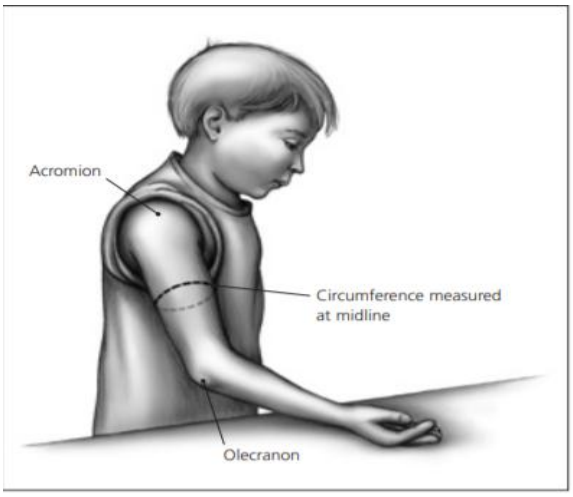

Figure 1. Arm circumference should be measured midway between the olecranon and acromial process.

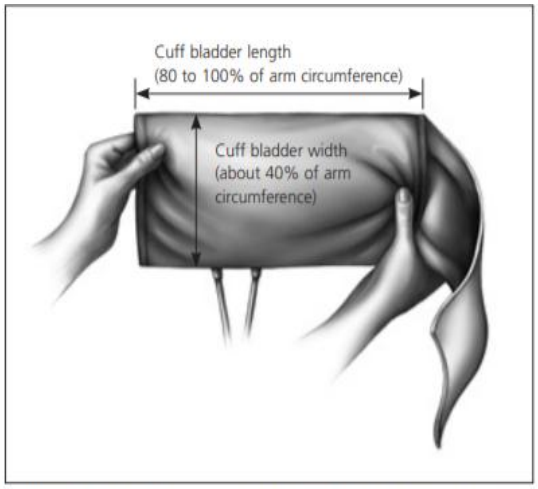

Figure 2. Blood pressure cuff showing size estimation based on arm circumference.

ETIOLOGIES:

Most childhood hypertension, particularly in preadolescents, is secondary to an underlying disorder. Renal parenchymal disease is the most common (60 to 70 percent) cause of hypertension. Adolescents usually have primary or essential hypertension, making up 85 to 95 percent of cases. Essential hypertension rarely is found in children younger than 10 years and is a diagnosis of exclusion. Significant risk factors for essential hypertension include family history and increasing BMI. Some sleep disorders and black race can be potential risk factors for essential hypertension. Essential hypertension often is linked to other risk factors that make up metabolic syndrome and can lead to cardiovascular disease. These risk factors for metabolic syndrome include low plasma high-density lipoprotein, elevated plasma triglycerides, abdominal obesity, and insulin resistance/hyperinsulinemia. The prevalence of metabolic syndrome among adolescents is between 4.2 and 8.4 percent. Secondary hypertension is more common in children than in adults. It can present in adolescents, especially if they have physical findings not typically seen with essential hypertension. Renal disease is the most common cause of secondary hypertension in children. Other causes include endocrine disease (e.g., pheochromocytoma, hyperthyroidism) and pharmaceuticals (e.g., oral contraceptives, sympathomimetics, some over-the counter preparations, dietary supplements). Transient rise in blood pressure, which can be mistaken for hypertension, is seen with caffeine use and certain psychological disorders (e.g., anxiety, stress).

EVALUATION:

Once hypertension has been confirmed, an extensive history and careful physical examination should be conducted to identify underlying causes of the elevated blood pressure and to detect any end-organ damage. With the appropriate information, unnecessary and often expensive laboratory and imaging studies can be avoided. The NHBPEP has developed an algorithm to help the physician navigate the diagnostic and management choices in childhood hypertension. History and physical examination as mentioned previously, the child with primary hypertension often has a positive family history of hypertension or cardiovascular disease. Other risk factors including metabolic syndrome and sleep-disordered breathing (from snoring to obstructive sleep apnea) also are associated with primary hypertension. A careful history will uncover these important elements. It is helpful to remember that secondary hypertension is more likely in a younger child with stage 2 hypertension, thus data about systemic conditions associated with elevated blood pressure should be elicited. Because most secondary hypertension is renovascular in origin, a focused review of that system may provide insight into the possible etiology. A medication history should include any use of over-the-counter, prescription, and illicit drugs because many medications and drugs can elevate blood pressure. The physician should also ask about the use of performance-enhancing substances, herbal supplements (e.g., ma huang), and tobacco use. Physical examination should include calculation of BMI because of the strong association between obesity and hypertension. Obtaining blood pressure readings in the upper and lower extremities to rule out coarctation of the aorta also is recommended. Examination of the retina should be included to assess the effect of hypertension on an easily accessed end organ. In the majority of children with hypertension, however, the physical examination will be normal.

TABLE 2
Physical Findings Indicative of a Secondary Cause for Childhood Hypertension

Physical examination finding	*Possible etiologies*
Abdominal bruit	Renal artery stenosis
Abdominal mass	Polycystic kidney disease; hydronephrosis/obstructive renal lesions; neuroblastoma; Wilms' tumor
Acne	Cushing's syndrome
Adenotonsillar hypertrophy	Sleep disorder associated with hypertension
Decreased perfusion of lower extremities	Coarctation of the aorta
Diaphoresis	Pheochromocytoma
Flushing	Pheochromocytoma
Growth retardation	Chronic renal failure
Hirsutism	Cushing's syndrome
Joint swelling	Systemic lupus erythematosus
Malar rash	Systemic lupus erythematosus
Moon facies	Cushing's syndrome
Murmur	Coarctation of the aorta
Muscle weakness	Hyperaldosteronism
Obesity (general)	Association with primary hypertension
Obesity (of the face, neck, or trunk)	Cushing's syndrome
Tachycardia	Hyperthyroidism; pheochromocytoma; neuroblastoma
Thyromegaly	Hyperthyroidism

TABLE 3
Causes of Childhood Hypertension According to Age Group

Age	*Causes*
One to six years	Renal parenchymal disease; renal vascular disease; endocrine causes; coarctation of the aorta; essential hypertension
Six to 12 years	Renal parenchymal disease; essential hypertension; renal vascular disease; endocrine causes; coarctation of the aorta; iatrogenic illness
12 to 18 years	Essential hypertension; iatrogenic illness; renal parenchymal disease; renal vascular disease; endocrine causes; coarctation of the aorta

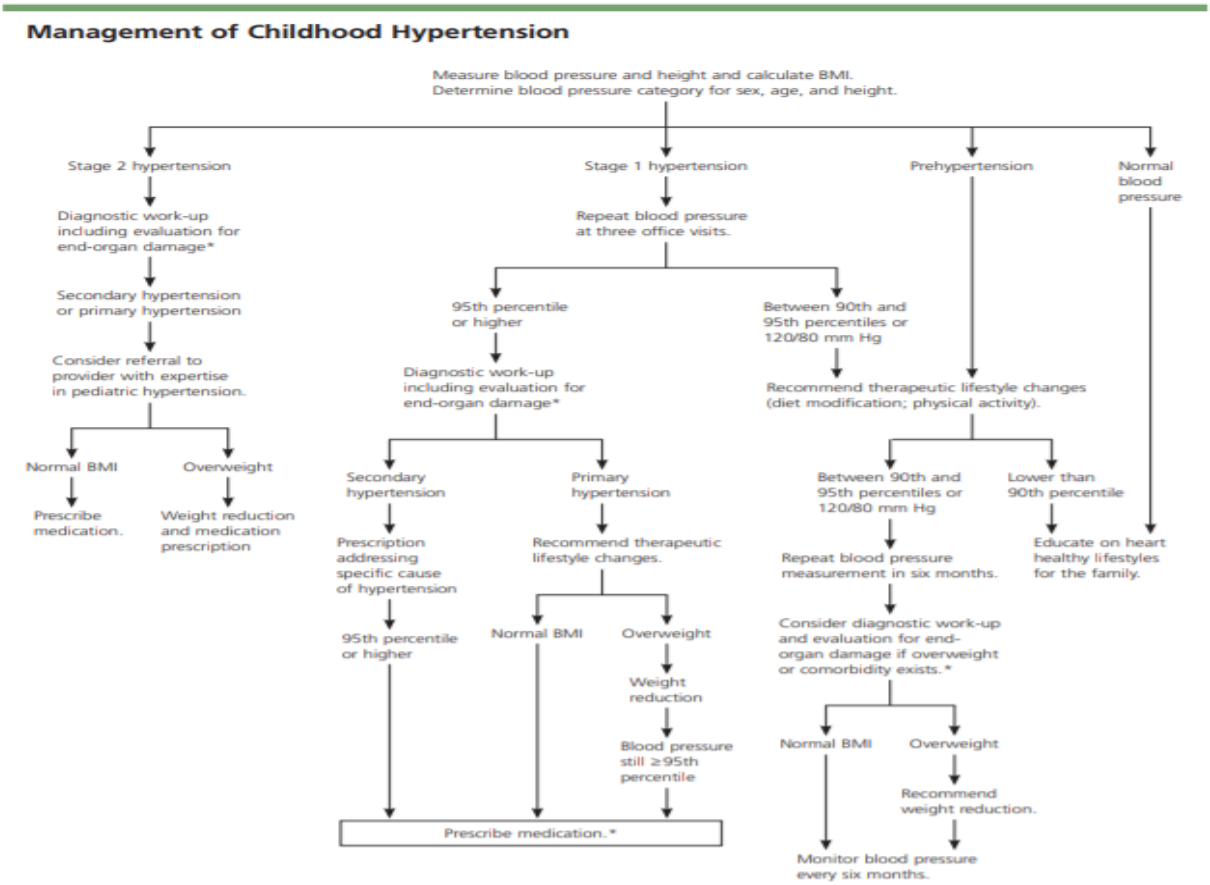

Figure 3. Algorithm for the management of childhood hypertension. (BMI = body mass index.)

Adapted with permission from National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 2004;114(2 suppl 4th report):571.

LABORATORY AND IMAGING TESTS:

Laboratory testing and imaging on a child with hypertension should screen for identifiable causes, detect comorbid conditions, and evaluate end-organ damage Screening tests should be performed on all children with a confirmed diagnosis of hypertension. Decisions about additional testing are based on individual and family histories, the presence of risk factors, and the results of the screening tests. Young children, those with stage 2 hypertension, and those in whom a systemic condition is suspected require a more extensive evaluation because these children are more likely to have secondary hypertension. The child who is older or obese, with a family history of diabetes or other cardiovascular risk factors, will require further work-up for the metabolic abnormalities associated with primary hypertension. Hormone levels and 24-hour urine studies are readily available to most physicians, but more specialized tests such as renal angiography often require referral to a centre with paediatric radiology, nephrology, and cardiology services. When renovascular disease is strongly suspected, conventional or intra-arterial digitally subtracted angiography are recommended. Scintography with or without angiotensin-converting enzyme (ACE) inhibition also can be used. These older imaging techniques are quite invasive. Data on newer

studies such as magnetic resonance angiography and 3-dimensional or spiral computed tomography in children are limited, but documentation of their usefulness is increasing. In addition to the diagnostic tests already mentioned, an assessment of end-organ damage must be made. Retinopathy, microalbuminuria, and increased carotid artery thickness have all been reported in children with primary hypertension. Documenting LVH is an important component of the evaluation of children with hypertension. Because echocardiography is noninvasive, easily obtained, and more sensitive than electrocardiography,it should be part of the initial evaluation of all children with hypertension and may be repeated periodically.

TABLE 4
History Suggesting Possible Etiologies or Associations with Hypertension

	Possible etiology and/or associations
Family history	
Cardiovascular disease (e.g., myocardial infarction, stroke)	Primary hypertension
Deafness	Congenital or familial renal disease
Dyslipidemia	Primary hypertension
Endocrine problems (e.g., diabetes, thyroid, adrenal)	Familial endocrinopathies
Hypertension	Primary hypertension
Kidney disease	Congenital or familial renal disease
Sleep apnea	Primary hypertension
Child's history	
Chest pain	Cardiovascular disease
Diaphoresis (abnormal)	Endocrinopathies
Dyspnea on exertion	Cardiovascular disease
Edema	Cardiovascular disease
Enuresis	Renovascular disease, renal scarring
Growth failure	Endocrinopathies
Heat or cold intolerance	Endocrinopathies
Heart palpitations	Cardiovascular disease
Headaches	Primary hypertension
Hematuria	Renovascular disease, renal scarring
Joint pain or swelling	Rheumatologic disorders
Myalgias	Rheumatologic disorders
Neonatal hypovolemia/shock	Renovascular disease, renal scarring
Recurrent rashes	Rheumatologic disorders
Snoring or other sleep problems	Primary hypertension
Umbilical artery catheterization	Renovascular disease, renal scarring
Urinary tract infections (recurrent)	Renovascular disease, renal scarring
Weight or appetite changes	Endocrinopathies

Information from reference 7.

TABLE 5
Laboratory Tests for the Child with Hypertension

Reason to test	*Tests*	*Purpose of result*
To identify cause	Complete blood count with differential, platelets	Rule out anemia, consistent with chronic renal disease
	Electrolytes, blood urea nitrogen, creatinine, calcium, phosphorus, uric acid	Rule out renal disease, calculi; chronic pyelonephritis
	Renal ultrasound	Rule out renal scarring; congenital renal anomalies; unequal renal size
	Urinalysis, urine culture	Rule out infection; hematuria; proteinuria
To identify comorbidities	Drug screen	Identify drug-induced hypertension
	Fasting lipid panel, fasting glucose, insulin	Identify hyperlipidemias, metabolic syndrome, or diabetes
	Polysomnography	Identify sleep disorders associated with hypertension
To identify end-organ damage	Echocardiography	Identify left ventricular hypertrophy
	Retinal examination	Identify retinal vascular changes
Additional testing (as clinically indicated)	24-hour urine for protein and creatinine, creatinine clearance	Rule out chronic renal disease
	Advanced imaging: renal scan; magnetic resonance angiogram; duplex Doppler flow studies; 3-dimensional computed tomography; arteriography (classic or digital subtraction)	Rule out renovascular disease
	Ambulatory blood pressure monitoring	Rule out physician anxiety-induced ("white-coat") hypertension
	Hormone levels (thyroid, adrenal)	Rule out hyperthyroidism, adrenal dysfunction
	Plasma renin levels	Rule out mineralocorticoid-related disease
	Urine and plasma catecholamines	Rule out catecholamine-mediated hypertension

MANAGEMENT:

Managing childhood hypertension is directed at the cause of the elevated blood pressure and the alleviation of any symptoms. End-organ damage, comorbid conditions, and associated risk factors also influence decisions about therapy. Non pharmacologic and pharmacologic treatments are recommended based on the age of the child, the stage of hypertension, and response to treatment.

NONPHARMACOLOGIC TREATMENTS:

For children and adolescents with pre-hypertension or stage 1 hypertension, therapeutic lifestyle changes are recommended. These include weight control, regular exercise, a low-fat and low-sodium diet, smoking cessation, and abstinence from alcohol use. Obesity increases the occurrence of hypertension threefold while favoring the development of insulin resistance, hyperlipidemia, and salt sensitivity. Significant obesity also increases the likelihood of LVH independent of blood pressure level. Exercise has been shown to lower blood pressure in children but does not affect left ventricular function. Competitive sports are permitted for children with prehypertension, stage 1 hypertension, or controlled stage 2 hypertension in the absence of symptoms and end-organ damage. Data regarding dietary changes in children with hypertension are limited. Nevertheless, the NHBPEP has taken an aggressive stance on

sodium restriction, recommending a sodium intake of 1,200 mg per day. A no-salt-added diet with more fresh fruits and vegetables combined with low-fat dairy and protein akin to the DASH (Dietary Approaches to Stop Hypertension) food plan30 may be successful in lowering blood pressure in children. Increased intake of potassium and calcium also have been suggested as nutritional strategies to lower blood pressure. Whatever lifestyle changes are recommended, a family-centered rather than patient oriented approach usually is more effective.

PHARMACOTHERAPY:

Reasons to initiate antihypertensive medication in children and adolescents include symptomatic hypertension, end-organ damage (e.g., LVH, retinopathy, proteinuria), secondary hypertension, stage 1 hypertension that does not respond to lifestyle changes, and stage 2 hypertension. In the absence of end-organ damage or comorbid conditions, the goal is to reduce blood pressure to less than the 95th percentile for age, height, and sex. When end-organ damage or coexisting illness is present, a blood pressure goal of less than the 90th percentile is recommended. Drug therapy is always an adjunct to nonpharmacologic measures. Information about long-term, untreated childhood hypertension and the impact of antihypertensive medications on growth and development is insubstantial. According to the NHBPEP, pharmacotherapy should follow a step-up plan, introducing one medication at a time at the lowest dose, then increasing the dose until therapeutic effects are seen, side effects are seen, or the maximal dose is reached. Only then should a second agent, preferably one with a complementary mechanism of action, be initiated. Long-acting medication is useful in improving compliance, and predictable problems such as the effect of diuretic medications in young athletes should be avoided.The choice of initial drug therapy is largely at the discretion of the physician. Diuretics and beta blockers have documented safety and effectiveness in children. Preferential use of specific classes of medications for certain underlying or coexisting pathology has led to the prescribing of ACE inhibitors in children with diabetes or proteinuria and beta-adrenergic or calcium channel blockers for children with migraines. Becoming familiar with medications in each major class and with effective combinations of medications will facilitate treatment. Many medications have growing research to support their use.As with any chronic health issue, medical follow-up and appropriate monitoring are key to long-term success.

Table 445-7 Recommended Doses for Selected Antihypertensive Agents for Use in Hypertensive Children and Adolescents

CLASS	DRUG	STARTING DOSE	INTERVAL	MAXIMUM DOSE*
Aldosterone receptor antagonist	Eplerenone	25 mg/day	qd-bid	100 mg/day
	Spironolactone†	1 mg·kg^{-1}·day^{-1}	qd-bid	3.3 mg·kg^{-1}·day^{-1} up to 100 mg/day
Angiotensin-converting enzyme inhibitors	Benazepril†	0.2 mg·kg^{-1}·day^{-1} up to 10 mg/day	qd	0.6 mg·kg^{-1}·day^{-1} up to 40 mg/day
	Captopril†	0.3-0.5 mg/kg/dose	bid-tid	6 mg·kg^{-1}·day^{-1} up to 450 mg/day
	Enalapril†	0.08 mg·kg^{-1}·day^{-1}	qd	0.6 mg·kg^{-1}·day^{-1} up to 40 mg/day
	Fosinopril	0.1 mg·kg^{-1}·day^{-1} up to 10 mg/day	qd	0.6 mg/kg/day up to 40 mg/day
	Lisinopril†	0.07 mg·kg^{-1}·day^{-1} up to 5 mg/day	qd	0.6 mg/kg/day up to 40 mg/day
	Quinapril	5-10 mg/day	qd	80 mg/day
Angiotensin receptor blockers	Candesartan	1-6 yr, 0.2 mg·kg^{-1}·day^{-1} 6-17 yr, <50 kg 4-8 mg once daily >50 kg 8-16 mg qdqd	qd	1-6 yr, 0.4 mg/kg; 6-17 yr, <50 kg 16 mg qd; >50 kg 32 mg qd
	Losartan†	0.75 mg·kg^{-1}·day^{-1} up to 50 mg/day	qd	1.4 mg·kg^{-1}·day^{-1} up to 100 mg/day
	Olmesartan	20 to <35 kg 10 mg qd; ≥35 kg 20 mg qd	qd	20 to <35 kg 20 mg qd ≥35 kg 40 mg qd
	Valsartan†	6-17 yr, 1.3 mg/kg/day up to 40 mg/day; <6 yr: 5-10 mg/day	qd	6-17 yr, 2.7 mg·kg^{-1}·day^{-1} up to 160 mg/day; <6 yr: 80 mg/day
α- and β-Adrenergic antagonists	Labetalol†	2-3 mg·kg^{-1}·day^{-1}	bid	10-12 mg·kg^{-1}·day^{-1} up to 1.2 g/day
	Carvedilol	0.1 mg/kg/dose up to 12.5 mg bid	bid	0.5 mg/kg/dose up to 25 mg bid
β-adrenergic antagonists	Atenolol†	0.5-1 mg·kg^{-1}·day^{-1}	qd-bid	2 mg·kg^{-1}·day^{-1} up to 100 mg/day
	Bisoprolol/HCTZ	0.04 mg·kg^{-1}·day^{-1} up to 2.5/6.25 mg/day	qd	10/6.25 mg/day
	Metoprolol	1-2 mg·kg^{-1}·day^{-1}	bid	6 mg·kg^{-1}·day^{-1} up to 200 mg/day
	Propranolol	1 mg·kg^{-1}·day^{-1}	bid-tid	16 mg·kg^{-1}·day^{-1} up to 640 mg/day
Calcium channel blockers	Amlodipine†	0.06 mg·kg^{-1}·day^{-1}	qd	0.3 mg·kg^{-1}·day^{-1} up to 10 mg/day
	Felodipine	2.5 mg/day	qd	10 mg/day
	Isradipine†	0.05-0.15 mg/kg/dose	tid-qid	0.8 mg·kg^{-1}·day^{-1} up to 20 mg/day
	Extended-release nifedipine	0.25-0.5 mg·kg^{-1}·day^{-1}	qd-bid	3 mg·kg^{-1}·day^{-1} up to 120 mg/day
Central α-agonist	Clonidine†	5-10 μg/kg/day	bid-tid	25 μg/kg/day up to 0.9 mg/day
Diuretics	Amiloride	5-10 mg/day	qd	20 mg/day
	Chlorthalidone	0.3 mg·kg^{-1}·day^{-1}	qd	2 mg·kg^{-1}·day^{-1} up to 50 mg/day
	Furosemide	0.5-2.0 mg/kg/dose	qd-bid	6 mg·kg^{-1}·day^{-1}
	HCTZ	0.5-1 mg·kg^{-1}·day^{-1}	qd	3 mg·kg^{-1}·day^{-1} up to 50 mg/day
Vasodilators	Hydralazine	0.25 mg/kg/dose	tid-qid	7.5 mg·kg^{-1}·day^{-1} up to 200 mg/day
	Minoxidil	0.1-0.2 mg·kg^{-1}·day^{-1}	bid-tid	1 mg·kg^{-1}·day^{-1} up to 50 mg/day

Table 445-8 Antihypertensive Drugs for Management of Severe Hypertension in Children 1–17 Yr

DRUG	CLASS	DOSE	ROUTE	COMMENTS
USEFUL FOR SEVERELY HYPERTENSIVE PATIENTS WITH LIFE-THREATENING SYMPTOMS				
Esmolol	β-Adrenergic blocker	100-500 μg/kg/min	IV infusion	Very short acting—constant infusion preferred. May cause profound bradycardia
Hydralazine	Direct vasodilator	0.2-0.6 mg/kg/dose	IV, IM	Should be given q4h when given IV bolus
Labetalol	α- and β-adrenergic blocker	bolus: 0.20-1.0 mg/kg/dose, up to 40 mg/dose infusion: 0.25-3.0 mg/kg/hr	IV bolus or infusion	Asthma and overt heart failure are relative contraindications
Nicardipine	Calcium channel blocker	Bolus: 30 mcg/kg up to 2 mg/dose Infusion: 0.5-4 μg/kg/min	IV bolus or infusion	May cause reflex tachycardia
Sodium nitroprusside	Direct vasodilator	0.5-10 μg/kg/min	IV infusion	Monitor cyanide levels with prolonged (>72 hr) use or in renal failure; or coadminister with sodium thiosulfate
USEFUL FOR SEVERELY HYPERTENSIVE PATIENTS WITH LESS-SIGNIFICANT SYMPTOMS				
Clonidine	Central α-agonist	0.05-0.1 mg/dose, may be repeated up to 0.8 mg total dose	PO	Side effects include dry mouth and drowsiness
Enalaprilat	ACE inhibitor	5-10 μg/kg/dose up to 1.25 mg/dose	IV bolus	May cause prolonged hypotension and acute renal failure, especially in neonates
Fenoldopam	Dopamine receptor agonist	0.2-0.8 μg/kg/min	IV infusion	Produced modest reductions in BP in a pediatric clinical trial in patients up to 12 yr
Hydralazine	Direct vasodilator	0.25 mg/kg/dose up to 25 mg/dose	PO	Extemporaneous suspension stable for only 1 wk
Isradipine	Calcium channel blocker	0.05-0.1 mg/kg/dose up to 5 mg/dose	PO	Stable suspension can be compounded
Minoxidil	Direct vasodilator	0.1-0.2 mg/kg/dose up to 10 mg/dose	PO	Most potent oral vasodilator; long acting

BOX I IMPORTANT CHANGES/NEW STATEMENTS IN THE CLINICAL PRACTICE GUIDELINE ON ELEVATED BLOOD PRESSURE BY AMERICAN ACADEMY OF PEDIATRICS, 2017

- New blood pressure charts for boys and girls.
- Blood pressure classification has been revised.
- Stepwise guidelines given for managing children with increased blood pressure (BP).
- Increased stress on importance of Ambulatory blood pressure monitoring (ABPM) in diagnosis and management of childhood hypertension
  - ABPM has been strongly recommended for confirming a diagnosis of hypertension (HTN) in children and adolescents if they have office BP measurements in the elevated BP category for 1 year or more or with stage 1 HTN over 3 clinic visits.
  - ABPM should be done for suspected White-coat hypertension or Masked hypertension.
  - Its use was particularly recommended in special group of populations such as chronic kidney disease and post transplantation.
- Children ≥6 y of age were recommended to not routinely require extensive investigation for secondary causes of HTN if they have a positive family history of HTN, are overweight or obese, and/or do not have history or physical examination findings suggestive of a secondary cause of HTN.
- Monogenic HTN should be suspected in patients with a family history of early-onset HTN, hypokalemia, suppressed plasma renin, or an elevated Aldosterone Renin Ratio (ARR).
- Renovascular HTN should be suspected in children with stage 2 HTN, significant diastolic HTN, discrepant kidney sizes on ultrasound, hypokalemia on screening investigations, or an epigastric and/or upper abdominal bruit on physical examination.
- Electrocardiogram not recommended for assessing left ventricular hypertrophy.
- Echocardiography strongly recommended to assess for target organ damage at the time of consideration of pharmacologic treatment of HTN.
- Doppler renal ultrasonography may be useful in evaluation of renal artery stenosis in normal weight children and adolescents ≥8 years of age who will cooperate with the procedure.
- Indication to initiate treatment
  - In hypertensive children and adolescents who have failed lifestyle modifications.
  - Those with target organ damage such as left ventricular hypertrophy.
  - Symptomatic HTN, or stage 2 hypertension without a clearly modifiable factor (eg, obesity).
- Target BP: Reduction in systolic BP and diastolic BP to <90th percentile
- Beta blocker should not be used as initial anti- hypertensive. Usual choice of anti-hypertensive should include ACEi, ARB, long-acting calcium channel blocker, or thiazide diuretic.

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Anti-NMDA encephalitis –A case Report

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ABSTRACT

Anti-N-methyl-D-aspartate receptor encephalitis is well characterized immune-mediated encephalitis. It is increasingly being recognized as one of the common causes of encephalitis, but is frequently misdiagnosed especially in resource-constrained settings. With a simple test available to diagnose the disorder and prospects of good recovery following early immunotherapy, the disorder should be kept as a differential diagnosis in patients presenting with unexplained behavioral/psychiatric symptoms and progressive encephalopathy with movement disorders.

CASE

A 7 year old female child presented to our emergency department with chief complaints of 2 episodes of seizures consisting of involuntary focal movements of right hand persists for around 2 minutes, associated with up rolling of eyes and right side deviation of mouth, self limited with a gap between two seizure episodes of around 4 hours. There was a history of poor sleep, irritability and difficulty in answering questions, intermittent tonic right hand rotations. On further enquiry, mother revealed history of right involuntary focal moments 3 weeks back, admitted in a local hospital and managed as meningitis with partial treatment for 7 days and discharged against medical advice on oral dose of Levetiracetam. Currently, child presented after 2 weeks with similar focal involuntary movements associated with behavioral/psychiatric symptoms.

On examination, child is oriented to time, place, person and has short term memory disturbance with difficulty in answering questions. Her cranial nerve, motor, sensory examination is normal. There were no meningeal signs, however, she has intermittent tonic involuntary rotation of right hand. She was investigated to rule out TB meningitis, vasculitis, partially treated meningitis, auto immune encephalitis. She was started on antibiotics and Levetiracetam.

CSF analysis showed pleomorphic leucocytosis with neutrophil predominance and normal protein.MRI brain demonstrated acute on chronic meningitis picture.EEG showed frequent generalized epileptiform discharges of frequency 3-4 hz/ sec. On 2nd day of admission, child had further episodes of right focal

involuntary movements lasting for about 3 to 5 minutes. She was commenced on Phenytoin and oral Oxcarbazepine for seizure control. She had a Pediatric Neurologist review who suspected Auto-immune Encephalitis and started her on steroids (IV Dexamethasone) for 5 days followed by slow taper for 3 weeks with oral prednisolone .She showed significant clinical response following steroid therapy with no recurrence of involuntary movements but continued to have irritable behavior, intermittent tongue fasiculations, insomnia.CSF analysis for Tuberculosis was negative. However, blood and CSF Auto immune panel was turned out to be positive for anti-NMDA encephalitis. Child was then started on IVIG with a dose of 2grams/kg given as two divided doses and continued on tapering doses of oral prednisolone. Following IVIg therapy, child showed signs of gradual recovery in involuntary movements, behavior disturbances/psychiatric symptoms .Child was discharged later with a plan to gradual weaning of steroids and anti-epileptics on further follow up.

DISCUSSION

Anti-NMDAR encephalitis is a relatively rare diagnosis with just a few hundred cases reported in the Literature but its true prevalence, especially in individuals with purely psychiatric manifestations, is yet to be determined, as a large majority present to a psychiatrist first .NMDARs play a central role in synaptic transmission helping to modulate human memory, cognition and learning and have been implicated in neuralplasticity. Activity of the NMDAR is affected not only by several exogenous substances, including PCP, ketamine, and ethanol, but also endogenous brain immune interactions that can have tremendous clinical consequences. The structure of the NMDAR is composed primarily of ubiquitous NR1 and NR2 subunits. The antibodies in anti-NMDAR encephalitis are directed against an epitope found on the NR1 subunit primarily in the fronto-temporal and hippocampal regions likely owing to the high density of these receptors in these regions. This geographic pattern helps explain common psychiatric signs and symptoms seen in this disease, including decreased cognition and personality changes.

The psychiatric manifestation of anti-NDMAR encephalitis syndrome is preceded by a nonspecific prodromal stage that can include headaches, low-grade fevers, diarrhea, or upper respiratory infection symptoms. This is followed by prominent psychiatric changes like anxiety, paranoia, mania, hyper-religiosity, delusions, and hallucinations that initiate within 2 weeks. Short-term memory loss evaluation is hindered by accompanying language deficits from echolalia to mutism. Neuromotor dysfunction with ataxia and choreiform movements and autonomic instability may also occur as the disease progresses. Complex seizures present relatively early but overlap between epileptiform movements and oro-facial dyskinesias may present a clinical dilemma in proper identification.

Brain MRI has been reportedly negative in up to 50–70% of patients. When irregularities are seen, it is often subtle T2 or FLAIR sequence hyperintensities in the hippocampal, fronto basal, insular, or basal

ganglia regions. EEG may show abnormal slowing, but is non-specific in 90% of patients and there is no role for brain biopsy in diagnosis. Current diagnosis is based upon finding anti-NMDAR antibodies in the CSF or serum. CSF studies show lymphocytic pleocytosis and normal to mild elevation of protein. Oligoclonal bands may be present in 60% of patients. Although there is controversy between testing for serum or CSF antibody titers, CSF titers generally appear to correlate with disease activity. The CSF antibody has been found to be more sensitive but there are still some explanations for why one might find a falsely negative result. This may include smaller quantities of antibodies produced, antigen denaturation during tissue based immune fixation and variability between human and mouse epitopes used in analysis. In our patient serum antibodies were tested which was positive associated with clinical symptoms suggestive of auto-immune encephalitis which responded well to the treatment.

Immuno modulation and neoplasm removal targeting both symptomatic and causal factors are mainstays of treatment. Immunotherapy such as with steroids, plasmapheresis and IVIG helps reduce antibody titers. Benzodiazepines and antipsychotics round out the pharmaco therapies employed in the treatment of seizures, psychosis and behavioral dysfunction. Recovery from illness following treatment is generally good with up to 75% of patients achieving full recovery or left with minimal residual deficits. Severe disability may result in the remaining 25%with mortality rates of 4–7%. Reported relapse rates range between 12% and 24%, more often in those without teratoma.

Prognosis is guarded and disease can often be lethal with irreversible damage to cortical regions such as the hippocampus in those who experience delay in identification and treatment. Independent predictors of good clinical outcome include time to identification and treatment, admission not requiring ICU care, and lesser initial symptomatology.

CONCLUSION

Anti-NMDAR encephalitis is an increasingly recognized, potentially lethal syndrome of psychiatric and neuro motor dysfunction in patients, often younger in age, who have an underlying neoplasm. Diagnosis is challenging and misdiagnosis is frequent given overlap of symptoms with multiple other infectious, neuroanatomic and psychiatric disease processes, and nonspecific or unremarkable findings on lumbar puncture, EEG, and neuro imaging. Early identification, immunotherapy, and malignancy work-up are the mainstays of management. Delays in these steps are dangerous as approximately 1 in 4 patient send up with debilitating neuropsychiatric dysfunction or death, even with appropriate treatment. Clinicians, at the very least, should entertain this diagnosis in patients with acute neuropsychiatric deterioration, CSF with lymphocytic pleiocytosis, and otherwise unrevealing cranial imaging and metabolic testing.

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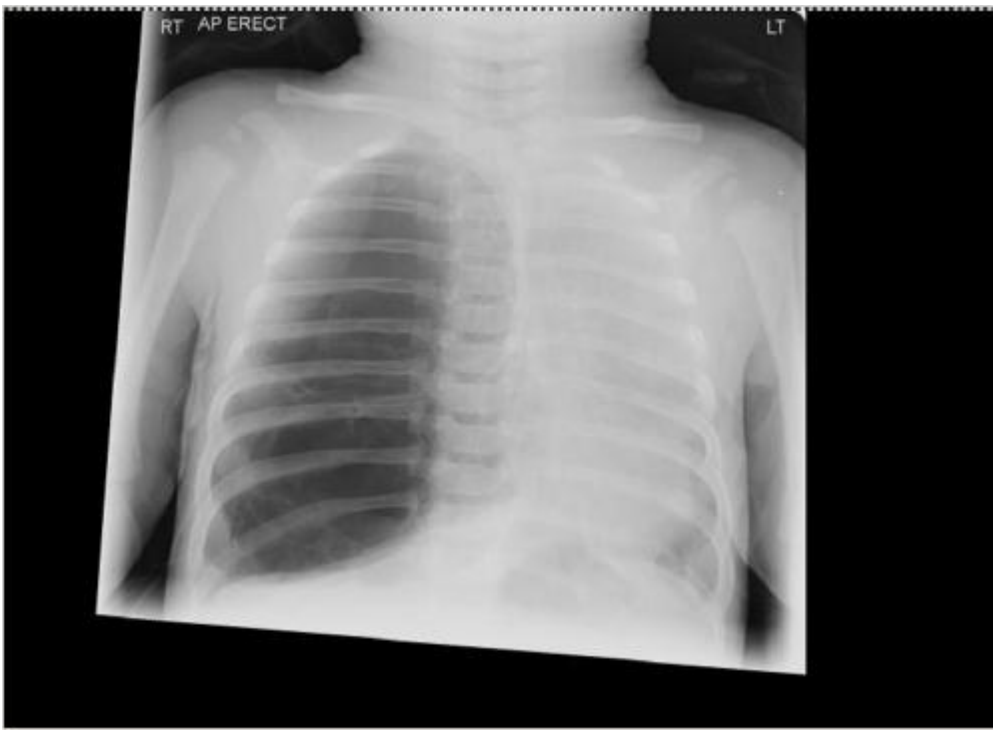
A 3 month old baby was admitted to the paediatric unit with a history of poor weight gain and tachypnoea. She was born at 39+1 weeks gestation by normal vaginal delivery following an unremarkable pregnancy. Her birth weight plotted on the 75th centile, but had gradually drifted down to the 9th centile where it plotted on the day of admission. Her mother had concerns that her work of breathing had increased over the previous few days, she struggled to feed and was only able to take 40 mls of milk per feed. She had not been coryzal or pyrexial. On examination she was pink and well perfused with normal heart sounds and normal femoral pulses. There was moderate sub-costal and intercostal recession and head bobbing. Auscultation of the chest revealed reduced air entry on the right with no added sounds. Heart sounds were normal. Her abdomen was soft and a 1e2 cm liver edge was palpable.A chest X-ray was performed and is shown below



1. What is the most likely cause for the chest X-ray appearances?

The patient remained tachypnoeic with a respiratory rate of 60 breaths per minute. Her heart rate was 146 beats per minute, blood pressure 112/72, temperature 36.6 C and Saturations 97% on air. Her CXR was discussed with the radiology team and further investigations arranged

2. What further investigations would you like to perform?

3. What complications would you expect from this condition if it was left untreated?

Answers:

1. Right sided Congenital pulmonary airway malformation (CPAM)
2. ECHO, Renal Ultrasound, HRCT Chest
3. Recurrent pneumonia ,pneumothorax and Malignant transformation

Congenital pulmonary airway malformation (CPAM), formerly known as congenital cystic adenomatoid malformation (CCAM) is a congenital anomaly of the lung which results in the development of abnormal cystic pulmonary tissue, usually in one lobe of the lung. This cystic tissue is unable to function in the same way as normal lung tissue. As the malformation increases in size, it may compress surrounding structures. Definitive treatment involves surgical resection of the abnormal tissue and usually involves a lobectomy. Smaller lesions may be managed conservatively. CPAM is often seen and diagnosed on antenatal ultrasound scans. If not seen on antenatal ultrasound scans, infants may present with signs of respiratory distress or pneumonia. CT chest imaging assesses the extent of the malformation and identifies the morphology of microcystic or macrocystic appearances. High resolution CT (HRCT) chest imaging is usually performed. Renal ultrasound and echocardiography should also be performed to exclude any other congenital malformations. The abnormally functioning lung tissue leads to an increased susceptibility of recurrent pneumonia. This may be a presenting feature in a child not previously known to have CPAM. Air trapping within the cystic tissue can also lead to a spontaneous pneumothorax and should be considered in a patient with conservatively managed CPAM presenting with shortness of breath and chest pain. There is a risk of malignant transformation of the abnormal lung tissue in later childhood or adulthood. Although the risk of this is small, surgical intervention is often preferred to conservative management for this reason.