Condylomata acuminatum in the prepubescent child: Report of case

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Condylomata acuminatum is common in the adult population. However, when reported in the prepubescent child, it should be considered with a high index of suspicion since it may be a subtle sign of extensive child abuse, as in the case reported. Child abuse is stereotyped as the battered child syndrome, but sexual abuse is being more frequently recognized in today's children. It is not associated with typically blatant physical abuse, but rather, subtle threats and psychologic trauma. Most of the previous reports of prepubescent condylomata in the literature have overlooked the association with abuse. While there is evidence of noncoital epidemiology, condylomata in prepubescent children is more likely to be associated with child abuse. The assistance of a multidisciplinary team can be helpful to the physician, the family, and the child in both recognition of the problem and initiation of therapy.

There are few reports in the literature of condylomata acuminatum in children. Of these, most either reported a congenital transmission of the virus or have not commented on the mode of transmission. Recently, perhaps because of increasing concern for children's welfare, there have been reports of condylomata acuminatum as a result of sexual molestation.[1,2] Transmission of these lesions are well documented in the adult population, especially by the venereal route. It has not been widely appreciated that condylomata in the prepubescent child may suggest child abuse. Because of this, the finding should be approached with a high degree of suspicion and be evaluated from a social, as well as medical, standpoint. This is a report of a child who presented with such findings. Only after persistent investigation by both medical personnel and social service was a history of sexual abuse elicited.

Report of case

A 5-year-old black female presented to the emergency room with a complaint of acute perineal bleeding. Her mother related that this was the result of her falling in bed and hitting a bedrail. Abuse or sexual contact was denied. Physical examination at that time revealed a minor laceration of the labia minora with friable condylomata of the perineum and labia. Cultures and serologic evaluations were performed and, on recommendation from the gynecology service, therapy for condylomata acuminatum was deferred. A child abuse report was filed with state and local agencies and a return visit was requested in 1 week.

At the return visit, the mother said that the patient admitted to having been the victim of several sexual assaults over the past several months. The mother's boyfriend had been reported as the perpetrator. The mother also related a change in the patient's behavior; she was quiet, sleeping poorly, and complaining of painful urination. Serologic evaluations and cultures for gonorrhea were negative from the emergency room visit. Appropriate medical therapy was instituted for condylomata, and the family was referred to a local counselling service.

Review of literature

The literature on condylomata acuminatum in children is sparse. The explanations of transmission in children seem to mostly delete the important aspect, that of coital contact. Patel and Groff [3] reported a case of an 18-month-old girl who presented with white vaginal discharge, bloody drainage, and a large cauliflower-like condylomata of the labia and hymen. This child was born to a mother who had been treated for condylomata in the last trimester of pregnancy. The lesion, which had been present for approximately 5 months, was treated with a combination of surgery and podophyllin. This case was the first English language report of a probable congenital transmission of

condylomata. Previous cases had not confirmed preexisting maternal condylomata. Later, Tang[4] suggested that congenital condylomata might be disseminated hematogenously, as well as by contiguity. He reported a case of a premature infant born to a mother with condylomata. Her intact fetal membranes were hypothesized to prevent ascending transmission.

Goldman and coworkers[5] reported on three children, 14 months to 16 years in age, with condylomata. In two, it was noted that an adult in the respective family had condylomata; in the third (a 16-year-old male), it was noted that he also had periungual verrucae. No explanation of the mode of transmission is offered in this communication; however, it is implied that condylomata acuminatum may be transmitted in a family in a fashion similar to verruca vulgaris and verruca plantaris. Storrs[1] followed up Goldman's letter. He reported on two children with condylomata who were strongly suspected of being victims of sexual molestation by family members. It was suggested that Goldman reevaluate his cases for the possibility of abuse.

Stumpf[6] reviews three cases. He noted a six-year-old and two five-year-olds with a later onset of condylomata acuminatum. In two cases, there was no history of family members with condylomata. He suggested that these cases were examples of an epidemic-like spread into the pediatric population, "because more adults in more family units are carrying the infection." He further stated that noncoital transmission is likely because the parents "denied direct genital contact."

The first documented report in the English language literature of condylomata from child abuse was by Seidel and associates.[2] He reported four cases of condylomata, three of which were admitted to be associated with sexual abuse. None of these children presented with complaints of sexual abuse; rather, the presenting complaints included warts on the vagina, rectal bleeding, pain on defecation, and blood stains on underwear secondary to "falling on a rock." Only after further investigation by social agencies were histories of sexual contact elicited. The authors further recommend screening these children with VDRL and cultures of pharynx, rectum, and genital areas for gonorrhea.

Discussion

Modern literature is replete with discussion of the transmission of condylomata. The etiologic agent is a papilloma virus, which is morphologically similar to, but antigenically different from, verruca vulgaris. Incubation periods vary from 6 weeks to 8 months. It has been documented that these lesions may be transmitted by sexual contact and congenitally. Noncoital transmission of the virus has not been conclusively demonstrated in spite of reports of such in the literature. Congenital transmission in the newborn has been substantiated by convincing circumstantial evidence. Stumpf[6] reviewed 22 cases in prepubertal children who denied direct genital contact with infected individuals. Although it is suggested that these cases were the result of epidemic exposure, the possibility of sexual contact is neither explored in depth nor eliminated.

The case study presented here is not remarkably different from those of Seidel.[2] It is significant that the child reported sexual abuse from a maternal paramour. Other reports might have produced such information, had there been suspicion from the investigators.

Sexual abuse in children is not uncommon; it may involve any kind of sexual act between the child and an adult. There may be isolated instances or repeated abuse. The prepubertal child is often left confused and disturbed following these instances. It should be remembered that when children finally discuss this event, they rarely make up stories about sexual abuse.[7]

When examining a child with condylomata acuminatum, the physician should maintain a high index of suspicion. A history of sexual contact rarely is obtained in the initial interview. If sexual contact is denied upon questioning, further investigations need to be considered. Social agencies are often more attuned to dealing with this type of problem.[8] It would not be unusual, as demonstrated by Seidel,[2] that further interviews with the family and child will reveal a history of the illness. While protection of the child is the principal goal, comprehensive family therapy is mandated. Social services demonstrate value with the initiation of therapy. The family may be more attuned to a cooperative relationship with the assistance of a social worker. The medical needs of the patient include appropriate management of the condylomata, as well as screening for other venereal diseases.

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3. Patel, R., and Groff, D.B.: Condyloma acuminata in childhood. Pediatrics 50:153-4, Jul 72

4. Tang, C.K., Shermeta, D.W., and Wood, C.: Congenital condylomata acuminata. Am J Obstet Gynecol 131:912, 1978

5. Goldman, L., Feldman, M., and Levitt, S.: Condyloma acuminata in infants and children [letter]. Arch Dermatol 112:1329, Sep 76

6. Stumpf, P.G.: Increasing occurrence of condylomata acuminata in premenarchal children. Obstet Gynecol 56:262-4, Aug 80

7. Kempe, C.H.: Sexual abuse, another hidden pediatric problem. The 1977 C. Anderson Aldrich lecture. Pediatrics 62:382-9, Sep 78

8. Bittner, S., and Newberger, E.H.: Pediatric understanding of child abuse. Pediatrics Rev 2:197-207, 1981

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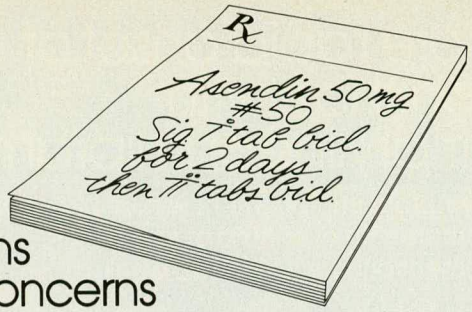

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DESCRIPTION
ASENDIN *amoxapine* is an antidepressant of the dibenzoxazepine class, chemically distinct from the dibenzazepines, dibenzocycloheptenes, and dibenzoxepines.

It is designated chemically as 2-chloro-11-(1-piperazinyl)dibenz-[b,f] [1,4]oxazepine. The molecular weight is 313.8. The empirical formula is $C_{17}H_{16}ClN_3O$.

ASENDIN is supplied for oral administration as 50 mg, 100 mg, and 150 mg tablets.

CLINICAL PHARMACOLOGY
ASENDIN is an antidepressant with a mild sedative component to its action. The mechanism of its clinical action in man is not well understood. In animals, amoxapine reduced the uptake of norepinephrine and serotonin and blocked the response of dopamine receptors to dopamine. Amoxapine is not a monoamine oxidase inhibitor.

ASENDIN is absorbed rapidly and reaches peak blood levels approximately 90 minutes after ingestion. It is almost completely metabolized. The main route of excretion is the kidney. *In vitro* tests show that amoxapine binding to human serum is approximately 90%.

In man, amoxapine serum concentration declines with a half-life of eight hours. However, the major metabolite, 8-hydroxyamoxapine, has a biologic half-life of 30 hours. Metabolites are excreted in the urine in conjugated form as glucuronides.

Clinical studies have demonstrated that ASENDIN has a more rapid onset of action than either amitriptyline or imipramine. The initial clinical effect may occur within four to seven days and occurs within two weeks in over 80% of responders.

INDICATIONS AND USAGE
ASENDIN is indicated for the relief of symptoms of depression in patients with neurotic or reactive depressive disorders as well as endogenous and psychotic depressions. It is indicated for depression accompanied by anxiety or agitation.

CONTRAINDICATIONS
ASENDIN is contraindicated in patients who have shown prior hypersensitivity to dibenzoxazepine compounds. It should not be given concomitantly with monoamine oxidase inhibitors. Hyperpyretic crises, severe convulsions, and deaths have occurred in patients receiving tricyclic antidepressants and monoamine oxidase inhibitors simultaneously. When it is desired to replace a monoamine oxidase inhibitor with ASENDIN, a minimum of 14 days should be allowed to elapse after the former is discontinued. ASENDIN should then be initiated cautiously with gradual increase in dosage until optimum response is achieved. The drug is not recommended for use during the acute recovery phase following myocardial infarction.

WARNINGS
ASENDIN should be used with caution in patients with a history of urinary retention, angle-closure glaucoma or increased intraocular pressure. Patients with cardiovascular disorders should be watched closely. Tricyclic antidepressant drugs, particularly when given in high doses, can induce sinus tachycardia, changes in conduction time, and arrhythmias. Myocardial infarction and stroke have been reported with drugs of this class.

Extreme caution should be used in treating patients with a history of convulsive disorder or those with overt or latent seizure disorders.

PRECAUTIONS
General: In prescribing the drug it should be borne in mind that the possibility of suicide is inherent in any severe depression, and persists until a significant remission occurs; the drug should be dispensed in the smallest suitable amount. Manic depressive patients may experience a shift to the manic phase. Schizophrenic patients may develop increased symptoms of psychosis; patients with paranoid symptomatology may have an exaggeration of such symptoms. This may require reduction of dosage or the addition of a major tranquilizer to the therapeutic regimen. Antidepressant drugs can cause skin rashes and/or "drug fever" in susceptible individuals. These allergic reactions may, in rare cases, be severe. They are more likely to occur during the first few days of treatment, but may also occur later. ASENDIN should be discontinued if rash and/or fever develop. Amoxapine possesses a degree of dopamine-blocking activity which may cause extrapyramidal symptoms in <1% of patients. Rarely, symptoms indicative of tardive dyskinesia have been reported, possibly related to treatment with amoxapine.

Information for the patient: Patients should be warned of the possibility of drowsiness that may impair performance of potentially hazardous tasks such as driving an automobile or operating machinery.

Drug interactions: See "Contraindications" about concurrent usage of tricyclic antidepressants and monoamine oxidase inhibitors. Paralytic ileus may occur in patients taking tricyclic antidepressants in combination with anticholinergic drugs. ASENDIN may enhance the response to alcohol and the effects of barbiturates and other CNS depressants.

Therapeutic interactions: Concurrent administration with electroshock therapy may increase the hazards associated with such therapy.

Carcinogenesis, impairment of fertility: In a 21-month toxicity study at three dose levels in rats, pancreatic islet cell hyperplasia occurred with slightly increased incidence at doses 5–10 times the human dose. Pancreatic adenocarcinoma was detected in low incidence in the mid-dose group only, and may possibly have resulted from endocrine-mediated organ hyperfunction. The significance of these findings to man is not known.

Treatment of male rats with 5–10 times the human dose resulted in a slight decrease in the number of fertile matings. Female rats receiving oral doses within the therapeutic range displayed a reversible increase in estrous cycle length.

Pregnancy. Pregnancy category C: Studies performed in mice, rats, and rabbits have demonstrated no evidence of teratogenic effect due to ASENDIN. Embryotoxicity was seen in rats and rabbits given oral doses approximating the human dose. Fetotoxic effects (intrauterine death, stillbirth, decreased birth weight) were seen in animals studied at oral doses 3–10 times the human dose. Decreased postnatal survival (between days 0–4) was demonstrated in the offspring of rats at 5–10 times the human dose. There are no adequate and well controlled studies in pregnant women. ASENDIN should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing mothers: ASENDIN, like many other systemic drugs, is excreted in human milk. Because effects of the drug on infants are unknown, caution should be exercised when ASENDIN is administered to nursing women.

Pediatric use: Safety and effectiveness in children below the age of 16 have not been established.

ADVERSE REACTIONS
Adverse reactions reported in controlled studies in the United States are categorized with respect to incidence below. Following this is a listing of reactions known to occur with other antidepressant drugs of this class but not reported to date with ASENDIN.

INCIDENCE GREATER THAN 1%
The most frequent types of adverse reactions occurring with ASENDIN in controlled clinical trials were sedative and anticholinergic: these included drowsiness (14%), dry mouth (14%), constipation (12%), and blurred vision (7%).

Less frequently reported reactions were:
CNS and Neuromuscular—anxiety, insomnia, restlessness, nervousness, palpitations, tremors, confusion, excitement, nightmares, ataxia, alterations in EEG patterns.
Allergic—edema.
Gastrointestinal—nausea.
Other—dizziness, headache, fatigue, weakness, excessive appetite, increased perspiration.

INCIDENCE LESS THAN 1%
Anticholinergic—disturbances of accommodation, mydriasis, delayed micturition, urinary retention, nasal stuffiness.
Cardiovascular—hypotension, hypertension, syncope, tachycardia.
Allergic—drug fever with skin rash, photosensitization, pruritus, rarely vasculitis.
CNS and Neuromuscular—tingling, paresthesias of the extremities, tinnitus, disorientation, seizures, hypomania, numbness, incoordination, disturbed concentration, extrapyramidal symptoms, including, rarely, tardive dyskinesia.
Hematologic—leukopenia.
Gastrointestinal—epigastric distress, vomiting, flatulence, abdominal pain, peculiar taste, diarrhea.
Endocrine—increased or decreased libido, impotence, menstrual irregularity, breast enlargement and galactorrhea in the female.
Other—lacrimation, weight gain or loss, altered liver function.

DRUG RELATIONSHIP UNKNOWN
The following reactions have been reported very rarely, and occurred under uncontrolled circumstances where a drug relationship was difficult to assess. These observations are listed to serve as alerting information to physicians.
Allergic—urticaria and petechiae.
Anticholinergic—paralytic ileus.
Cardiovascular—atrial arrhythmias (including atrial fibrillation), myocardial infarction, stroke, heart block.
CNS and Neuromuscular—hallucinations, nightmares.
Hematologic—thrombocytopenia, purpura.
Gastrointestinal—parotid swelling.
Endocrine—change in blood glucose levels.
Other—pancreatitis, hepatitis, jaundice, urinary frequency, testicular swelling, anorexia.

ADDITIONAL ADVERSE REACTIONS
The following reactions have been reported with other antidepressant drugs, but not with ASENDIN.
Anticholinergic—sublingual adenitis, dilation of the urinary tract.
CNS and Neuromuscular—delusions, syndrome of inappropriate ADH secretion.
Hematologic—agranulocytosis, eosinophilia.
Gastrointestinal—stomatitis, black tongue.
Endocrine—gynecomastia.
Other—alopecia.

OVERDOSAGE
Signs and Symptoms
Initial toxic manifestations of ASENDIN overdosage typically are CNS effects: delirium, lethargy with diminished deep tendon reflexes, and/or seizures. Cardiovascular effects, when they occur, are usually limited to sinus tachycardia and transient minor EKG changes. Serious hypotension, hypertension, or cardiac arrhythmias are rare. Respiratory acidosis may develop following repeated seizures, and metabolic acidosis has been reported.

Important
Renal impairment may develop three to five days after substantial overdosage in patients who may appear otherwise recovered. Oliguria, hematuria, and renal failure have been reported. Tubular necrosis and rhabdomyolysis with myoglobinuria may also occur in such cases. Treatment is the same as that for non-drug-induced renal dysfunction. In a limited series of cases of renal failure following overdosage, 70% have recovered with appropriate treatment.

In general, treatment of overdosage must be symptomatic and supportive. If the patient is conscious, induced emesis followed by gastric lavage with appropriate precautions to prevent pulmonary aspiration should be accomplished as soon as possible. Following lavage, activated charcoal may be administered to reduce absorption. An adequate airway should be established in comatose patients and assisted ventilation instituted if necessary. Convulsions, should they occur, may respond to standard anticonvulsant therapy; however, barbiturates may potentiate any respiratory depression. Specific treatment should be guided by the predominant symptoms which may suggest use of a particular pharmacologic agent. For example, the slow intravenous administration of physostigmine salicylate has been reported to reverse most of the serious cardiovascular and CNS effects of overdosage with tricyclic antidepressants, such as cardiac arrhythmias and convulsions. (Avoid rapid injection to reduce the possibility of physostigmine-induced convulsions). Convulsions may also be treated with intravenous diazepam. Acidosis may be treated by cautious intravenous administration of sodium bicarbonate.

A patient who has ingested a toxic overdose of a tricyclic antidepressant may remain medically and psychiatrically unstable for several days due to sustained excessive drug levels. Unexpected cardiac deaths have occurred up to six days post-overdose with other antidepressants. The QRS interval of the electrocardiogram appears a reliable correlate of the severity of overdosage. If the QRS interval exceeds 100 milliseconds anytime during the first 24 hours after overdose, cardiac function should be continually monitored for five or six days. (Prolongation of the QRS interval beyond 100 milliseconds has not been reported with ASENDIN over-dosage, and there have been no deaths due to primary cardiac toxicity.)

The smallest estimated lethal overdose reported has been 2.6 grams. On the other hand, some patients have survived much larger overdoses. Age and physical condition of the patient, concomitant ingestion of other drugs, and especially the interval between drug ingestion and initiation of emergency treatment, are important determining factors in the probability of survival.

DOSAGE AND ADMINISTRATION
Effective dosage of ASENDIN may vary from one patient to another. Usual effective dosage is 200 mg to 300 mg daily. Three weeks constitutes an adequate period of trial providing dosage has reached 300 mg daily (or lower level of tolerance) for at least two weeks. If no response is seen at 300 mg, dosage may be increased, depending upon tolerance, up to 400 mg daily. Hospitalized patients who have been refractory to antidepressant therapy and who have no history of convulsive seizures may have dosage raised cautiously up to 600 mg daily in divided doses.

ASENDIN may be given in a single daily dose, not to exceed 300 mg, preferably at bedtime. If the total daily dosage exceeds 300 mg, it should be given in divided doses.

Initial Dosage for Adults: Usual starting dosage is 50 mg two or three times daily. Depending upon tolerance, dosage may be increased to 100 mg two or three times daily by the end of the first week. (Initial dosage of 300 mg daily may be given, but notable sedation may occur in some patients during the first few days of therapy at this level.) Increases above 300 mg daily should be made only if 300 mg daily has been ineffective during a trial period of at least two weeks. When effective dosage is established, the drug may be given in a single dose (not to exceed 300 mg) at bedtime.

Elderly Patients: In general, lower dosages are recommended for these patients. Recommended starting dosage of ASENDIN is 25mg two or three times daily. If no intolerance is observed, dosage may be increased by the end of the first week to 50 mg two or three times daily. Although 100–150 mg daily may be adequate for many elderly patients, some may require higher dosage. Careful increases up to 300 mg daily are indicated in such cases.

Once an effective dosage is established, ASENDIN may conveniently be given in a single bedtime dose, not to exceed 300 mg.

Maintenance: Recommended maintenance dosage of ASENDIN is the lowest dose that will maintain remission. If symptoms reappear, dosage should be increased to the earlier level until they are controlled.

For maintenance therapy at dosages of 300 mg or less, a single dose at bedtime is recommended.

HOW SUPPLIED
ASENDIN *Amoxapine* Tablets are supplied as follows:
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100 mg—Blue, heptagon-shaped tablets, engraved on one side with LL above 100 and with A17 on the other scored side.
(Product No. NDC 0005-5391-23)—bottles of 100
(Product No. NDC 0005-5391-60)—10 x 10 Unit Dose
150 mg—Peach, heptagon-shaped tablets, engraved on one side with LL above 150 and with A18 on the other scored side.
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