
Communications

Infectious Mononucleosis in Third Trimester of Pregnancy

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Infectious mononucleosis is a relatively common disease caused by Epstein-Barr virus in young women of child-bearing age.¹ Several case reports reveal infants with severe congenital stigmata resulting from maternal Epstein-Barr virus infections in the first trimester of pregnancy.²⁻⁴ Little appears to be known about infectious mononucleosis and its effects on a fetus in the third trimester of pregnancy. Because of the morphologic similarities of Epstein-Barr virus and the herpes virus group, the outcome of a pregnancy with documented Epstein-Barr virus in the third trimester would be of particular interest. The following is a case report of a maternal mononucleosis infection documented one week prior to delivery.

Case Report

T.W. was a 19-year-old married white woman, gravida 1. She had an uneventful pregnancy until the 36th week, when she had premature rupture of membranes with nitrazine-positive fluid. This leak sealed within two to three hours. The patient was hospitalized, monitored for contractions, and re-

leased after three days when serial white cell counts, endocervical cultures, and temperatures did not reveal evidence of amnionitis. She was then followed in the clinic on a twice-weekly basis for the next two weeks. At 38 weeks she complained of a sore throat, fatigue, myalgias, and swollen cervical lymph nodes at a routine visit. Physical examination showed her to have an erythematous throat without exudates and several 1- to 1.5-cm tender, mobile anterior cervical lymph nodes. The spleen could not be palpated and there was no skin rash. She had a negative streptococcal screen of the throat and a positive Monospot test. The white cell count was 5,100/mm³ with 37 percent lymphocytes and 12 percent atypical lymphocytes.

Six days later the patient had spontaneous onset of labor followed by spontaneous rupture of membranes. A 7 lb 11 oz boy was delivered vaginally. His Apgar scores were 6 at one minute and 9 at five minutes. The child had no abnormalities on physical examination. During his nursery stay, he had no problems with skin rash, respiratory distress, hypoglycemia, or temperature instability. The highest bilirubin value was 9.4 mg/100 mL at three days of age. His Monospot was negative, and there were no transformed lymphocytes on a peripheral smear of blood.

While hospitalized, the mother continued to have positive Monospot results and had 11 percent

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LIMBITROL® TABLETS *v* Tranquilizer—Antidepressant

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of moderate to severe depression associated with moderate to severe anxiety.

Contraindications: Known hypersensitivity to benzodiazepines or tricyclic antidepressants. Do not use with monoamine oxidase (MAO) inhibitors or within 14 days following discontinuation of MAO inhibitors since hyperpyretic crises, severe convulsions and deaths have occurred with concomitant use; then initiate cautiously, gradually increasing dosage until optimal response is achieved. Contraindicated during acute recovery phase following myocardial infarction.

Warnings: Use with great care in patients with history of urinary retention or angle-closure glaucoma. Severe constipation may occur in patients taking tricyclic antidepressants and anticholinergic-type drugs. Closely supervise cardiovascular patients. (Arrhythmias, sinus tachycardia and prolongation of conduction time reported with use of tricyclic antidepressants, especially high doses. Myocardial infarction and stroke reported with use of this class of drugs.) Caution patients about possible combined effects with alcohol and other CNS depressants and against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving).

Usage in Pregnancy: Use of minor tranquilizers during the first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Since physical and psychological dependence to chlordiazepoxide have been reported rarely, use caution in administering Limbitrol to addiction-prone individuals or those who might increase dosage; withdrawal symptoms following discontinuation of either component alone have been reported (nausea, headache and malaise for amitriptyline; symptoms [including convulsions] similar to those of barbiturate withdrawal for chlordiazepoxide).

Precautions: Use with caution in patients with a history of seizures, in hyperthyroid patients or those on thyroid medication, and in patients with impaired renal or hepatic function. Because of the possibility of suicide in depressed patients, do not permit easy access to large quantities in these patients. Periodic liver function tests and blood counts are recommended during prolonged treatment. Amitriptyline component may block action of guanethidine or similar antihypertensives. Concomitant use with other psychotropic drugs has not been evaluated; sedative effects may be additive. Discontinue several days before surgery. Limit concomitant administration of ECT to essential treatment. See Warnings for precautions about pregnancy. Limbitrol should not be taken during the nursing period. Not recommended in children under 12. In the elderly and debilitated, limit to smallest effective dosage to preclude ataxia, oversedation, confusion or anticholinergic effects.

Adverse Reactions: Most frequently reported are those associated with either component alone: drowsiness, dry mouth, constipation, blurred vision, dizziness and bloating. Less frequently occurring reactions include vivid dreams, impotence, tremor, confusion and nasal congestion. Many depressive symptoms including anorexia, fatigue, weakness, restlessness and lethargy have been reported as side effects of both Limbitrol and amitriptyline. Granulocytopenia, jaundice and hepatic dysfunction have been observed rarely.

The following list includes adverse reactions not reported with Limbitrol but requiring consideration because they have been reported with one or both components or closely related drugs:

Cardiovascular: Hypotension, hypertension, tachycardia, palpitations, myocardial infarction, arrhythmias, heart block, stroke.

Psychiatric: Euphoria, apprehension, poor concentration, delusions, hallucinations, hypomania and increased or decreased libido.

Neurologic: Incoordination, ataxia, numbness, tingling and paresthesias of the extremities, extrapyramidal symptoms, syncope, changes in EEG patterns.

Anticholinergic: Disturbance of accommodation, paralytic ileus, urinary retention, dilatation of urinary tract.

Allergic: Skin rash, urticaria, photosensitization, edema of face and tongue, pruritus.

Hematologic: Bone marrow depression including agranulocytosis, eosinophilia, purpura, thrombocytopenia.

Gastrointestinal: Nausea, epigastric distress, vomiting, anorexia, stomatitis, peculiar taste, diarrhea, black tongue.

Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement, galactorrhea and minor menstrual irregularities in the female and elevation and lowering of blood sugar levels.

Other: Headache, weight gain or loss, increased perspiration, urinary frequency, mydriasis, jaundice, alopecia, parotid swelling.

Overdosage: Immediately hospitalize patient suspected of having taken an overdose. Treatment is symptomatic and supportive. I.V. administration of 1 to 3 mg physostigmine salicylate has been reported to reverse the symptoms of amitriptyline poisoning. See complete product information for manifestation and treatment.

Dosage: Individualize according to symptom severity and patient response. Reduce to smallest effective dosage when satisfactory response is obtained. Larger portion of daily dose may be taken at bedtime. Single *h.s.* dose may suffice for some patients. Lower dosages are recommended for the elderly. Limbitrol 10-25, initial dosage of three to four tablets daily in divided doses, increased up to six tablets or decreased to two tablets daily as required. Limbitrol 5-12.5, initial dosage of three to four tablets daily in divided doses, for patients who do not tolerate higher doses.

How Supplied: White, film-coated tablets, each containing 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt) and blue, film-coated tablets, each containing 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt)—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 50.

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atypical lymphocytes. Both mother and child were discharged uneventfully at 72 hours.

Prior to the child's delivery there was concern about the possibility of a fetal Epstein-Barr virus (EBV) infection. Samples of maternal peripheral venous blood and the infant's cord blood were sent to the Mayo Clinic for Epstein-Barr virus titers. TORCH titers (toxoplasmosis, rubella, cytomegalovirus, and herpes simplex virus) were also done during the acute infection (Table 1).

The mother's serum contained both IgG and IgM antibodies to the EBV viral capsid antigen (VCA). This is compatible with an acute infection. The IgG-EA (early antigen) was quite high in the mother, indicating an active infection. This may also be found with an abortive infection without indirect immunofluorescence to viral capsid antigen or viral particles. The significance of IgG-EA is not clear at this time. The IgG-EBNA is an IgG antibody to Epstein-Barr virus nucleic acids. This is of particular interest, since it is usually not elevated until several months after the acute infection. The negative IgG-EBNA in this setting indicates a primary infection.⁵

The infant would be expected to show some degree of IgG-VCA and IgG-EA because of the transplacental crossing of IgG. IgM does not cross the placenta. That there was IgM-VCA in the infant's cord blood indicates there was a fetal Epstein-Barr virus infection.

TORCH infections, especially cytomegalovirus, can be remarkably similar to infectious mononucleosis and do not cause a positive Monospot. The mother had a rubella and herpes infection at an unknown time. Since she had a screening rubella titer in the first trimester of 1 to 80, an acute rubella infection was unlikely. She had no signs or symptoms of a herpes infection during pregnancy or of any other TORCH infection.

Unfortunately, both the mother and child were lost to follow-up after the six-week postpartum visit, and there were no convalescent titers. A telephone follow-up at three months revealed the child to be thriving and developing without problems. Further attempts at contact have been futile.

Epstein-Barr virus as a teratogen is a subject needing further investigation. This pregnancy, with a well-established diagnosis of third-trimester mononucleosis and a favorable outcome of the in-

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Table 1. Acute Viral Titers

	IgG-VCA	IgM-VCA	IgG-EA	IgG-EBNA	VDRL	Toxoplasmosis	Rubella	Cytomegalovirus	Herpes Simplex
Mother	160	>10	<10	Negative	Negative	Negative	1:55	<1:8	1:16
Infant	20	5	<10	Negative	Not done	Negative	1:27	<1:8	1:32

fectured infant within the confines of limited follow-up, adds to the existing knowledge of perinatal viral infections and their sequelae.

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Workplace Observation: Key to a Meaningful Office History

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As the workplace becomes more complex in terms of energy, automation, specialization, and chemicals, it becomes more difficult to obtain a good occupational history from the patient. A good history is defined as one the physician can understand and put to use for diagnosis, treatment, prevention, or rehabilitation.

Shortcomings of the Routine Work History

There are a number of difficulties with the standard approach to occupationally related health problems. Often the occupational history is taken as a lengthy questionnaire filled out by patients (with or without assistance) when they first visit.¹ The questionnaire is reviewed and then filed, usu-

ally not to be updated. When the physician tries to obtain a more detailed occupational history, the process is likely to be tedious, time consuming, and less than accurate. Patients vary in their ability to describe the workplace, especially if the physician does not know the appropriate questions to ask. In fact, the more complex, technical, or repetitive the task, the less revealing may be the worker's description. Each workplace has a terminology all its own that the physician may find confusing. Too often a work-related problem is missed because the physician decides, from an inadequate data base, that the workplace is not likely to be relevant in the disease process; the extra effort required to obtain a detailed occupational history is therefore deferred, delegated, or neglected. On the other hand, some workers ascribe to their jobs symptoms that are not work-related.²

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Observation at the Workplace

One way to improve the office-obtained occupational history is to train primary care physicians