Vulvar edema in pregnancy: A case report

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ABSTRACT

Isolated massive vulvar edema in pregnancy is rare. The causative mechanisms remain poorly understood but it is probably related to mechanical, osmotic and hormonal factors. The differential diagnoses of vulvar edema include infections, tumors, lymph birth defects, trauma, inflammatory and metabolic diseases. This is a case of a 24-year-old primigravid with twin pregnancy who was admitted at 24 weeks age of gestation for massive vulvar edema. Reported causes of vulvar edema were ruled out. The aim of this report is to discuss the clinical aspects, differential diagnosis, causes and evolution of vulvar edema in pregnancy.

Keywords: edema, twin pregnancy, vulva

INTRODUCTION

Edema is defined as abnormal and excessive accumulation of fluid within the skin. It is facilitated by any of the following factors: increased intravascular hydrostatic pressure, reduced plasma oncotic pressure, increased blood vessel wall permeability, obstructed lymphatic clearance of fluids, and, finally, changes in the water retention properties of tissue. Body areas with distensible and loose skin, including the genitalia, are common sites for edema formation. Depending on the underlying cause of edema, the resultant fluid accumulation is either of plasma or lymphatic origin and at times both.

Vulvar edema is associated with a variety of medical conditions. There are also several other vulvar conditions that closely mimic edema making it difficult at times to clearly differentiate these conditions from edema. Vulvar edema can be a diagnostic dilemma and a treatment challenge for health care providers while causing significant discomfort for affected individuals.

We report a case of a 24-year-old primigravid with twin pregnancy who was admitted at a tertiary government hospital at 24 weeks age of gestation for massive vulvar edema.

CASE REPORT

A 24-year-old primigravid at 24 weeks age of gestation with twin pregnancy was admitted at a tertiary government hospital with a chief complaint of swelling of the external genitalia for three days. She was known to have vitiligo since birth and was diagnosed with hyperthyroidism a year ago; however, no maintenance medication was taken. Her family, personal and social histories were unremarkable. She had her menarche at 16 years-old, with subsequent menstrual periods coming at regular intervals, lasting for 4 days and soaking 3-4 pads per day with no associated dysmenorrhea. Her last menstrual period was on November 17, 2018 giving her an amenorrhea of 24 weeks. She had 3 unremarkable prenatal check-ups at a local health center.

History of present illness started 2 days prior to consult, when the patient noted multiple tender pinpoint ulcers at the right labia majora, that caused limited mobility and difficulty voiding of the patient. No consult was done. A few hours prior to admission, she noted sudden massive swelling of the vulva prompting consult at our institution. Review of systems revealed palpitations, easy fatigability, 2-pillow orthopnea and heat intolerance. Upon arrival to the Emergency Room, she had a blood pressure of 130/70 mmHg, heart rate of 106 beats per minute, respiratory rate of 24 cycles per minute, temperature of 36.9, and oxygen saturation of 98%. On physical examination, she had exophthalmos, and multiple, well-defined, irregularly-shaped, hypopigmented patches on bilateral periorbital area (Figure 1). There was a diffusely enlarged, non-tender anterior neck mass measuring 5x4cm that moved with deglutition (Figure 2). On abdominal examination, fundic height was 22cm, a combined estimated fetal weight of 800 grams to 1000 grams, both twins were in cephalic in presentation with fetal heart tones ranging from 130-150 beats per minute. On pelvic examination, the vulva was markedly swollen and tender to touch with no lesions or discharge (Figure 3). Internal examination was not done due to the severe tenderness in vulvar area. She also

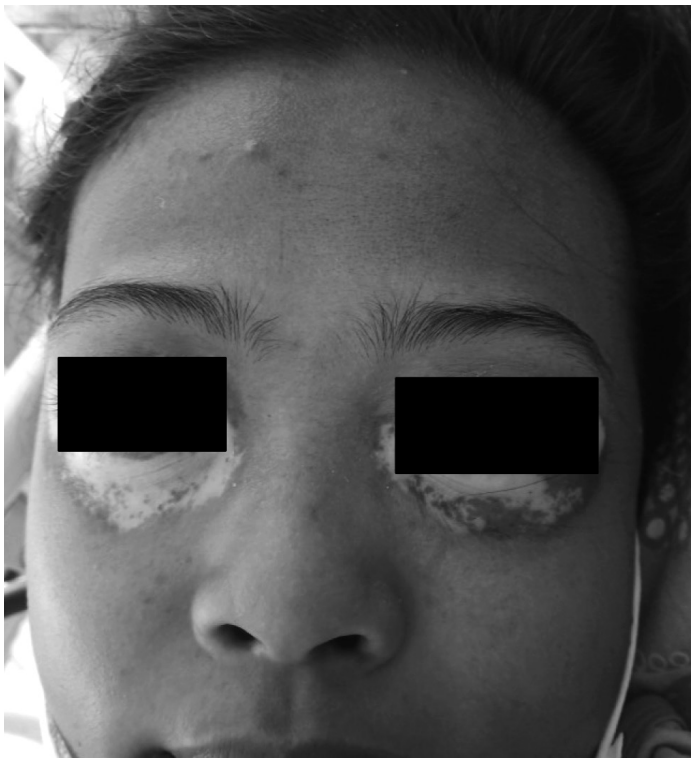

Figure 1. Localized hypopigmentation of bilateral periorbital areas

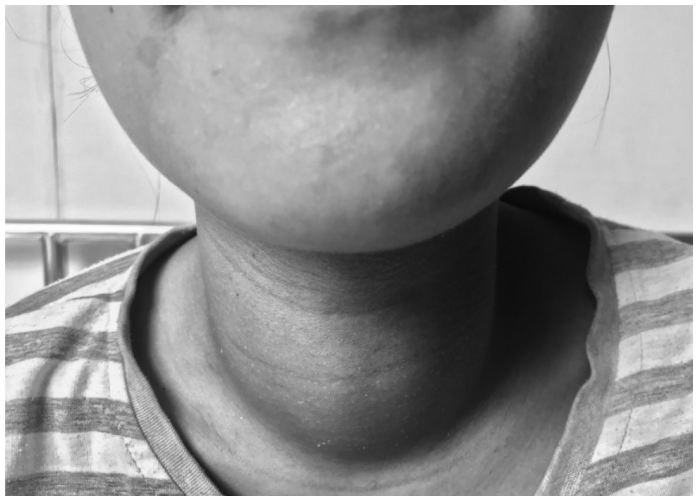

Figure 2. Anterior neck mass

presented with grade 2 non-pitting edema of the lower extremities.

Biometry on admission showed Twin live intrauterine pregnancy, both with good cardiac and somatic activities. Twin A: Cephalic presentation, 23 weeks by composite aging. Adequate amniotic fluid volume. Estimated fetal weight is appropriate for gestational age. Doppler studies of the umbilical artery show normal values. Provisional congenital anomaly scan shows cardiomegaly. Twin B: cephalic presentation, 22 4/7 weeks by composite aging. Adequate amniotic fluid volume. Estimated fetal weight is appropriate for

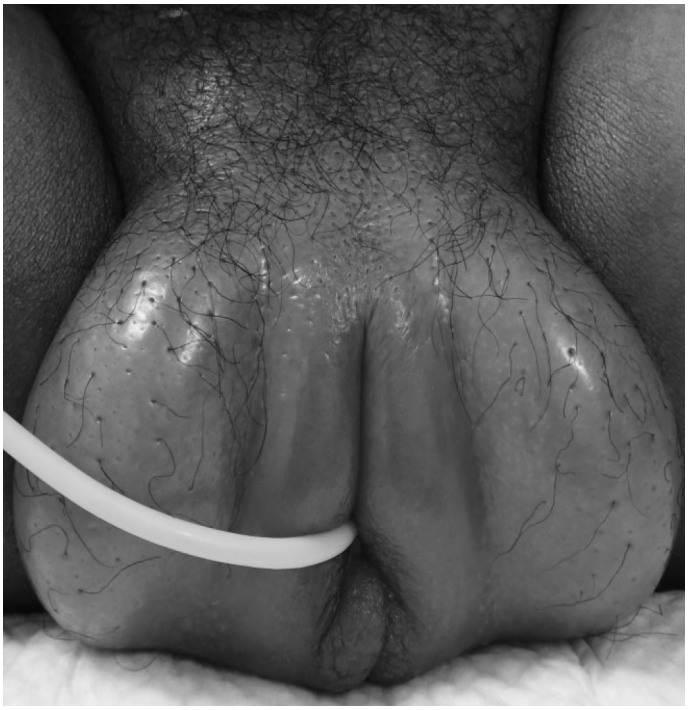

Figure 3. Photo showing massive vulvar edema. Indwelling foley catheter was inserted due to difficulty voiding

gestational age. Doppler flow studies of the umbilical artery show normal values. Congenital anomaly scan revealed cardiomegaly and dilated right atrium. Placenta is right posterolateral, high lying grade 1. Placentation appears monochorionic, diamnionic. Doppler flow studies of the uterine arteries show normal values for the right uterine artery. The left uterine artery show elevated values and exhibit early diastolic notching. (Figure 4).

Laboratory examinations revealed anemia, elevated FT4, decreased TSH and hypoalbuminemia. Tables 1 shows the results of all the laboratory examinations done during the admission. Referrals were done to general medicine as well as to the sections of endocrinology, cardiology, dermatology and infectious diseases for co-management.

Ferrous sulfate was increased to twice a day, while Human Albumin was given every 12 hours. Patient was diagnosed with diffuse toxic goiter probably Grave's Disease, biochemically and clinically hyperthyroid and heart failure functional class II probably from thyrotoxic heart disease, not in decompensation. She was then started on Methimazole 20mg/tab, one tablet to be taken twice a day and Propanolol 10mg/tablet 1 tablet once a day. Further workup was done including thyroid stimulating hormone receptor antibody (TRAb) and antinuclear antibody (ANA) tests to rule out other autoimmune diseases. A 75g OGTT was also done which revealed elevated results giving a diagnosis of

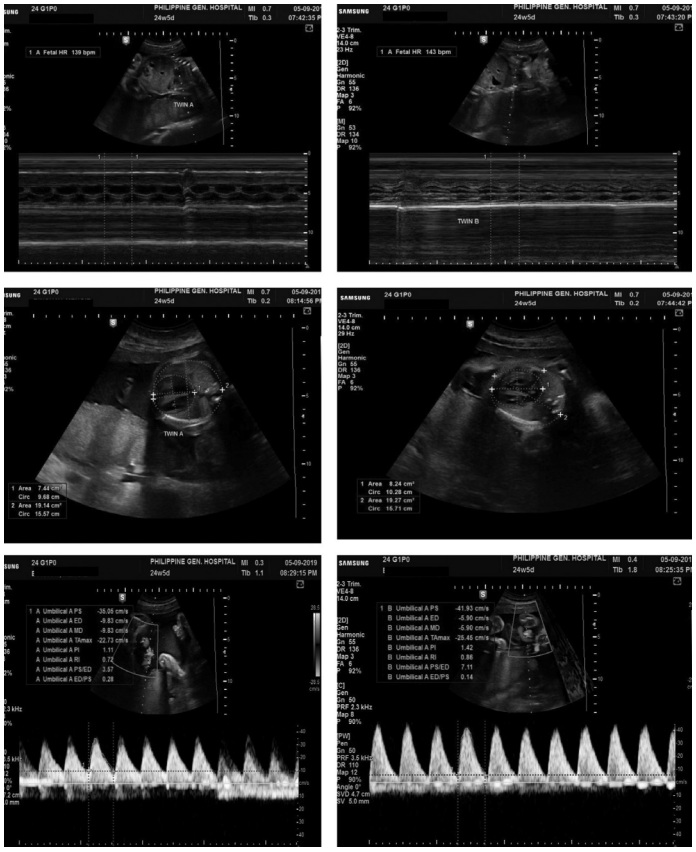

Figure 4. Ultrasound pictures of the twins

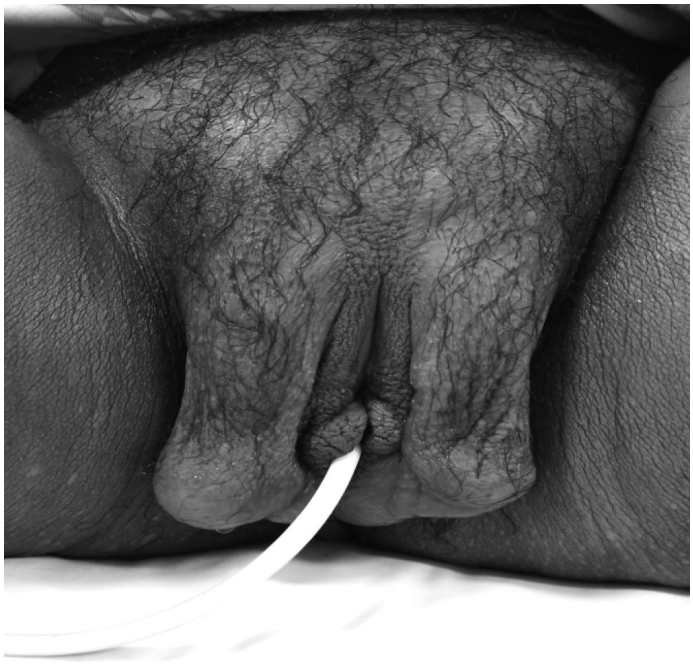

Figure 4. Photo showing regression of the massive vulvar swelling following spontaneous rupture

gestational diabetes mellitus. She was then started on NPH Insulin 30-0-6 units given subcutaneously pre-meals. Capillary blood glucose (CBG) monitoring was done thrice a day.

Patient was referred to the Section of Infectious Diseases to rule out any infectious cause of the vulvar swelling. However, after thorough history taking and physical examination and review of laboratory test results, an infectious cause of the vulvar swelling seemed unlikely. The Section on Dermatology advised corticosteroids as treatment for the Vitiligo and phototherapy postpartum. She was also referred to the Section of Cardiology regarding possible thyroid heart disease; 2D Echo with Doppler was done which revealed normal ejection fraction of 66% and cleared for any septal defects. She was started on Propanolol 10mg/tablet 1 tablet thrice a day for the palpitations.

On the 4th hospital day, there was increase in pain in the vulvar area followed by spontaneous rupture of the edema with egress of clear to yellowish watery discharge (Figure 5). During the interim, close monitoring and different laboratory and diagnostic workup were done to assess the cause of the vulvar edema. There was no re-accumulation of fluid thus patient was discharged improved after 14 days of hospitalization. She was advised regular follow-up checkup at our outpatient department.

The patient followed-up once at our outpatient department with no reported recurrence of the vulvar edema. She was advised to continue her maintenance medications and to follow-up with the Sections of Endocrinology and Cardiology. However, she was lost to follow-up.

At thirty-seven weeks and one day age of gestation, she was brought to the OB admitting section due to labor pains. Upon physical assessment, she was noted to have bilateral periorbital edema, and anterior neck mass and grade 1 edema of the lower extremities. Repeat thyroid function test was done which revealed normal FT4 and low TSH (Table 1). The progress of her labor was monitored closely and she eventually delivered via outlet forceps extraction of both twins, females with pediatric aging of 37 weeks and APGAR score of 9 remaining 9. Twin A weighed 2300 grams while twin B weighed 2400 grams, both were appropriate for gestational age. She was referred back to other co-managing services including Section of Endocrinology and Cardiology, which she was advised for continuation of medications and regular follow-up at the Outpatient department. The patient was also referred back to the section of Otolaryngology for biopsy of her anterior neck mass. She was then discharged with no recurrence of edema.

Table 1. Laboratory test results of the patient.

Complete Blood Count			
	5/8/2019	**5/10/2019**	**8/4/2019**
WBC Count	17.7 x 10^9/L	14.00 x 10^9/L	11.7 x 10^9/L
RBC Count	3.83 x 10^12/L	3.51 x 10^12/L ↓	4.41 x 10^12/L
Hemoglobin	101 g/L	94 g/L	139
Hematocrit	0.32	0.30	0.42
MCV	84.4 fL	84.7 fL	96 fL
MCH	26.3 pg	26.7 pg	31.4 pg
MCHC	312 g/L	315 g/L	327 g/L
RDW	14.7	15.0	16
Platelet Count	235 10^9/L	249 10^9/L	218 10^9/L
Neutrophils	0.74	0.75	0.65
Lymphocytes	0.12	0.14	0.22
Monocytes	0.13	0.10	0.12
Eosinophil	0.01	0.01	0.01
Basophil	0.00	0.00	0.00

Chemistry			
	5/8/2019	**5/10/2019**	**8/4/2019**
RBS	4.2 mmol/L		5.1 mmol/L
BUN	4.2 mmol/L		1.0 mmol/L
Creatinine	58 umol/L		37 umol/L
LDH	276 U/L		
AST	28 U/L ↓		19 u/L
ALT	13 IU/L		13 IU/L
Albumin	21 g/L	23 g/L ↓	32 g/L ↓
Sodium	132 mmol/L ↓		137 mmol/L
Potassium	4.9 mmol/L		3.5 mmol/L
Phosphorus	1.66 mmol/L		
Calcium	2.05 mmol/L		2.22 mmol/L
Magnesium	0.82 mmol/L		0.71 mmol/L
HbA1c	4.5%		4.5%
TRAB	>40 **(Positive)**		

Thyroid function test:				
	5/4/2019	**5/6/2019**	**5/15/2019**	**8/4/2019**
TSH	<0.005 ↓			0.0000 uiu/ml ↓
FT4	58.14 ↑		15.07 pmol/L	4.76 pmol/L
FT3	16.49 pmol/L ↑	6.04 pmol/L	4.74 pmol/L	14.17 pmol/L

4a. 2D Echocardiography: 5/8/2019 Eccentric left ventricular hypertrophy with adequate wall motion and contractility, with preserved overall systolic function, and Doppler evidence of indeterminate diastolic relaxation and abnormality. Dilated left atrium, normal right atrium, dilated right ventricle with normal contractility and systolic function. Structural normal valves. Moderate mitral regurgitation, trivial mitral regurgitation, pulmonic regurgitation. Elevated pulmonary artery pressures suggestive of pulmonary hypertension. IVC Plethora.
4b. 12 Lead ECG: 5/4/2019 Sinus tachycardia; Normal axis; Poor R wave progression
4c. Chest Xray PA: Impression: Left- sided cardiomegaly with pulmonary congestive changes
4d. Neck Ultrasound: Impression: Thyroid parenchymal disease with bilateral thyroid nodule.

CASE DISCUSSION

Edema is defined as the infiltration of abnormal or excess amounts of fluid in the connective tissues of the body. During pregnancy, the total body water increases by 6 to 8 L, with an estimated 4- to 6-L increase in extracellular compartments and 2- to 3-L increase in interstitial compartments. These large volume changes in addition to cumulative sodium retention lead to a decrease in oncotic pressure and increase in capillary pressure causing edematous changes in approximately 8 out of 10 pregnant women.[2]

Vulvar edema occurring during pregnancy requires careful evaluation for systemic disorders that may place both the patient and the baby at high risk for complications. There are several possible etiologies for development of vulvar edema in pregnancy:

1. Edema secondary to pregnancy

In pregnancy, greater water retention is normal and mediated in part by a drop in plasma osmolality of 10 mOsm/kg. This fluid accumulation, which may amount to a liter or so, results from greater venous pressure below the level of the uterus as a consequence of partial vena cava occlusion.[1] Any change in pressure and volume are quickly noticed in dependent areas such as the legs and in areas with substantial connective tissue, including the vulva. This results in pitting edema of the ankles and legs, and in some, vulvar edema. These were seen in our patient. Estrogen secretion during pregnancy is also believed to possibly alter the physicochemical characteristics of connective tissue mucopolysaccharides, allowing for a substantial increase in water storage. The vulva has large amounts of loose connective tissue and a thin epithelial layer allowing for an expansion of the interstitial space by fluids.[2]

The massive vulvar edema presented by the patient is very rare in normal pregnancy. Since her condition was associated with hyperthyroidism with possible heart failure, it is likely that the vulvar edema is not a result of pregnancy alone.

2. Cardiac disease secondary to thyroid disorder

The thyroid gland enlarges in pregnancy due to increased vascularity and cellular hyperplasia. Maternal thyroid function is modulated by three independent but interrelated factors: (i) an increase in thyroxin-binding globulin (TBG) during the first trimester, resulting in increased binding of thyroxin, (ii) an increase in the concentration of human chorionic gonadotropin (hCG), which exerts a thyroid stimulating hormone (TSH)-like activity, which stimulates the thyroid gland to produce thyroid hormone, and (iii) significant increase in urinary iodine excretion resulting in a fall in plasma iodine concentration.[3]

The prevalence of hyperthyroidism in pregnant women ranges from 0.05% to 0.2%. It is a condition that results from excess thyroid hormone, whether endogenous or exogenous, and is associated with characteristic signs and symptoms, which include exophthalmos, palpitations, tachycardia, heat intolerance and easy fatigability, all of which were present in our patient. The thyroid function test of our patient revealed elevated FT4 and decreased TSH, which supports the diagnosis of hyperthyroidism. Additionally, the patient had a positive TRAb test, which is indicative of Grave's disease resulting in hyperthyroidism.

Patients with severe hyperthyroidism may develop a high output heart failure. A study done by Chung-Wah Siu et al showed that congenital heart failure was the initial clinical presentation in approximately 6% of patients with hyperthyroidism with an annual incidence of 5.6 per 100,000 population.[5] The signs and symptoms are caused by increased cardiac output with normal systemic function and low systemic vascular resistance. The blood volume is increased due to activation of the renin angiotensin aldosterone system.[6] As a result, cardiac preload is enhanced. These changes were manifested by our patient as peripheral edema

on physical examination, left- sided cardiomegaly with pulmonary congestive changes, as seen in her chest x-ray, pulmonary hypertension, as seen in her 2-dimensional echocardiography. After initiating anti-thyroid medications there was improvement of the congestive circulatory symptoms as well as decrease in bipedal edema and absence of recurrence of the vulvar edema.

3. Hypoalbuminemia

During pregnancy, total serum calcium levels, which include both ionized and no-ionized calcium, decrease. This reduction follows lowered plasma album concentrations.[1] Hypoalbuminemia causes a decrease in oncotic pressure and a resultant maldistribution of body fluids into the interstitial spaces. The hypoalbuminemia of the patient is probably not the sole cause of patient's vulvar swelling since it usually presents with a more generalized third spacing edema.

4. Allergy

Edema can develop acutely on exposure to allergens, including topical medications, infections, and toxins. The resulting edema in these situations is termed, angioedema. This is a result of increased vascular permeability in response to mediators of inflammation. Generally, when acute angioedema occurs, onset of symptoms is often within minutes to hours and effects may last up to several days. Edema may be generalized or occasionally restricted to specific body sites, such as the vulva.[7] Even though the vulvar edema of the patient presented as an acute onset, allergic reaction is not highly considered since she did not present with pruritus, erythema, warmth. She also has no history of allergy to any food or medications or any exposure to toxins.

5. Infection (Genital Herpes)

Herpes simplex virus was acquired by 2 percent or more of susceptible women during pregnancy.10 The clinical diagnosis of genital herpes is based on typical painful crops of vesicles and ulcers in various stages of progression, with lesions lasting 3 to 6 weeks. While recurrent genital herpes infections are much milder and shorter with lesions lasting 3 to 10 days.[9] In primary genital herpes infection, there is tender inguinal adenopathy, fever and other constitutional symptoms may occur. The patient initially presented with multiple tender pinpoint ulcerations however based on her history; there is no noted fever or constitutional symptoms. Physical examination findings of the vulva showed severe edema however no vesicular or ulcerations noted

6. Mirror syndrome

Mirror syndrome, also referred to as Ballantyne's syndrome, is normally defined as the development of maternal edema in association with fetal hydrops. In a review of more than 50 cases of mirror syndrome, Braun (2010) found that approximately 90 percent of women had edema similar to the presentation of our patient.[1] However, on congenital anomaly scan, our patient did not present with hydrops fetalis. She also delivered normal twins at term and had no recurrence of vulvar edema after its spontaneous rupture and correction of her other medical conditions.

In evaluating the signs and symptoms, laboratory test results and clinical course of the patient, it would seem that the etiology of her massive vulvar edema is multifactorial. Although pregnancy causes edema due to the physiologic changes associated with the condition, her hypoalbuminemia and congestive heart failure secondary to thyrotoxicosis aggravated the edema. The massive vulvar edema may be the result of the large amount of connective tissue and loose skin in the area. Since tenderness in the area limited her mobility, she had to lie down most of the time thereby allowing fluid to collect in the area. Spontaneous rupture of the skin overlying the edema allowed the fluid collection to egress and correction of the medical complications prevented recurrence of the condition.

CONCLUSION

Vulvar edema has a wide range of causative factors and mechanisms. It is essential that the underlying etiology along with any associated medical conditions be identified for successful management. ■

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