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Lymphedema in Spina Bifida: A Case Series

Stanley G. Rockson, M.D., Amir Bahreman, M.D., Andrzej Szuba, M.D., Ph.D.

Division of Cardiovascular Medicine, Stanford University Lymphedema Center, Stanford University School of Medicine, Stanford, California

Abstract. Lymphedema is a chronic edematous state that can arise from any cause of low output failure of the lymphatic circulation. We herein present a series of three adult patients with spina bifida in whom the clinical diagnosis of lymphedema was also established. The diagnosis of spina bifida, with its attendant lower extremity inactivity, might intuitively suggest the presence of functional, dependent edema. However, imaging studies in one patient confirm a pattern of lymphatic malfunction that is virtually indistinguishable from the one that might accompany other, heritable forms of primary lymphedema. The important potential for lymphedema in spina bifida therefore warrants diagnostic scrutiny and therapeutic intervention in patients who develop edematous lower extremities, particularly in situations where the need for effective wound healing is heightened.

Introduction

Lymphedema is a chronic edematous state that can arise from any cause of low output failure of the lymphatic circulation. A long list of congenital and acquired causes of lymphedema has been elucidated [18]. These comprise both primary and secondary forms. Although many associations have been drawn between lymphedema and various congenital, acquired, and iatrogenic disease states, the potential relationship of lymphedema to neural tube defects has not previously been discussed. We herein present a series of three adult patients with spina bifida in whom the clinical diagnosis of lymphedema was also established.

A Report of Three Cases

During the period from 1996–1998, three adult patients presented to the University Lymphedema Center for evaluation of lower extremity edema in the setting of paraplegia based upon congenital spina bifida (Table 1). All three patients had presented with neonatal myelomeningocele and hydrocephalus with subsequent surgical repair, including ventriculoperitoneal shunt placement.

Of these three patients, one had received the diagnosis of lymphedema in childhood, while the others presented for an initial diagnostic evaluation of lower extremity edema in adulthood (ages 22 and 38, respectively). All of these patients had experienced genitourinary complications typical of spina bifida, such as neurogenic bladder, recurrent genitourinary infection, urolithiasis, and ureteroenteric fistula, but there were no additional distinguishing clinical features.

In all of these patients the lymphedema was moderate to severe, bilateral, symmetric, and generally indistinguishable from the morphology of typical primary lymphedema of the lower extremities. Stemmer's sign was present in all cases, and recurrent infection and ulceration was a universal feature in these patients. Patient 2 had a complete imaging evaluation of the edema: the indirect, ^{51}Tc-sulfur colloid lymphoscintigram documented an absence of iliofemoral lymph node visualization, along with typical dermal backflow in the distal calf region (Figure 1). This lymphoscintigraphic pattern is consistent with a severe impairment of peripheral lymphatic transport of the type that would be seen, for example, in hypoplasia or aplasia of the initial lymphatics.

All three patients were managed with conventional decongestive physiotherapy, including manual lymphatic drainage, bandaging, and application of compressive garments. With this therapy, substantial control of edema was accomplished and, in two of the three patients, the healing of active ulceration was facilitated.

Discussion

Neural tube defects are among the most common birth anomalies. Spina bifida comprises a wide range of these developmental abnormalities, including an absent spinous process, spina bifida occulta, myelomeningocele, and other malformations. Myelomeningocele, at times categorized as spina bifida aperta, spina bifida cystica, or myelodysplasia, is the most common open dysraphic malformation [7]. De-

Correspondence to: Stanley G. Rockson, M.D., Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, California 94305

Table 1. Patient characteristics

Patient	Age	Gender	Lymphedema Diagnosis (Age)	Cellulitis	Decubiti	Surgical Repair of Spina Bifida
1	29	F	Childhood	+	+	+
2	38	M	35	+	+	+
3	29	F	22	+	+	+

velopment of the neural tube begins in the third week of the gestation. Any defect in neurulation, the normal fusion of the neural folds at this stage of development, can result in the disturbances of structures that comprise the clinical substrate of spina bifida [7,12].

The prevalence of neural tube defects is distinctly related to such factors as geography [19,21], maternal socioeconomic status, dietary influences, and genetic factors [2]. Seasonal trends have been observed in some studies [4]. A recent decline in the incidence of the spina bifida has been ascribed to dietary modifications, prenatal screening, and selective termination of pregnancy [3,17].

Although the multifactorial etiology of spina bifida is well recognized [1,8,11], its exact pathogenesis is still incompletely understood. Maternal hyperthermia, parental occupation, antiepileptic drug use and maternal nutrition may all play a role [1,15]. Thus, folic acid deficiency is now well established as an important attributant [16], and trials of high-dose folic acid supplementation have successfully reduced the incidence of this disease [9,14].

There is a well-recognized association among spina bifida and a host of concomitant disorders [10]. The frequent appearance of hydrocephalus, hindbrain dysfunction, bladder dysfunction, hydromyelia, scoliosis [16], urolithiasis [6], cryptorchidism [5], and arachnoid cyst has been well documented in spina bifida patients. To date, no reference has been made to the association of spina bifida and chronic lymphedema of the lower extremities.

We herewith report a series of three adult patients with spina bifida and well-documented lymphedema, including one patient with lymphoscintographic documentation of lymphatic insufficiency in the lower extremities. The diagnosis of spina bifida and its attendant lower extremity inactivity might intuitively suggest the presence of functional, dependent edema. However, the imaging studies in patient 2 in fact confirm a pattern of lymphatic malfunction that is virtually indistinguishable from the one that might accompany other, heritable forms of primary lymphedema [18]. Although the mechanism of the association between lymphedema and the neural tube defect is not entirely clear, one can postulate a temporal association between intrauterine events that concomitantly affect the structural development of the nervous system and the lymphatic vasculature. Furthermore, an association between heritable developmental defects and both intrauterine and congenital lymphedema has been widely conjectured [13,20].

Although the inability to exercise the edematous limbs hampered the global applicability of decongestive therapy in these patients, it is nevertheless noteworthy that diligent use of manual lymphatic drainage, skin care, and compression led to remarkable amelioration in all three patients. The clinical response included the healing of significant cutaneous ulceration in two of the patients in this series. The important potential for lymphedema in spina bifida therefore warrants diagnostic scrutiny and therapeutic interven-

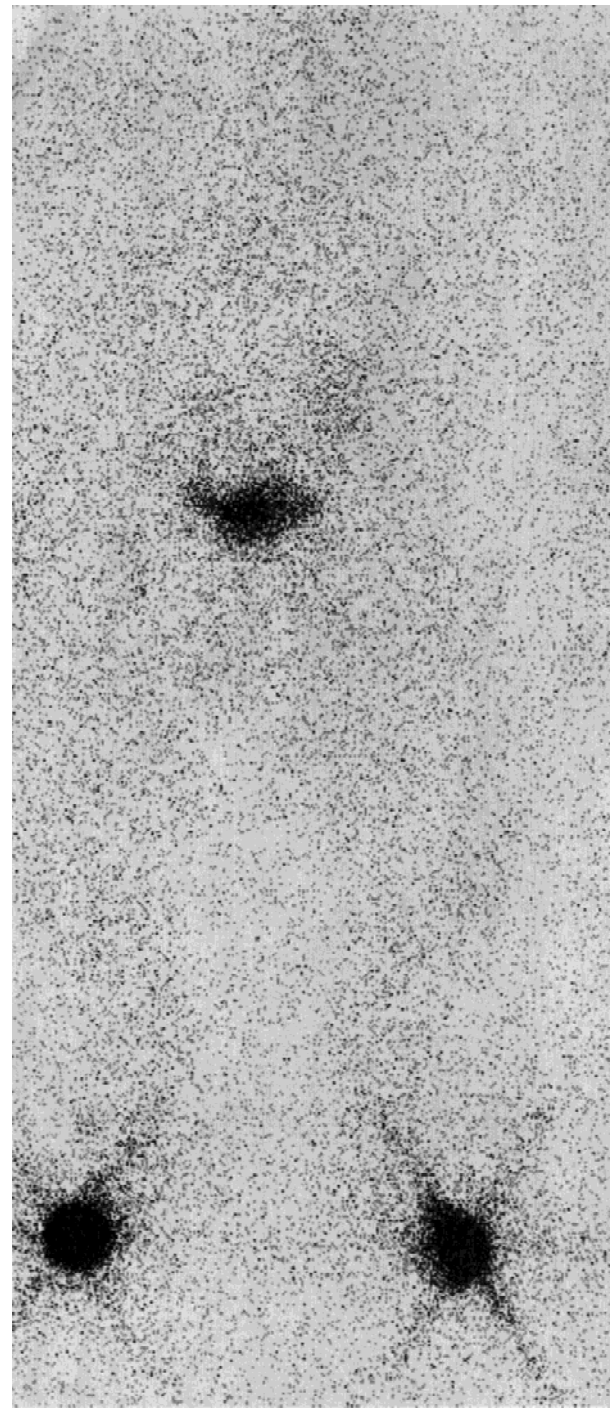

Fig. 1. Indirect radionuclide lymphoscintigraphy of the lower extremities was performed after bilateral intradermal injection of ^{51}Tc-sulfur colloid. The study documents an absence of iliofemoral lymph node visualization, along with typical dermal backflow in the distal calf region. This lymphoscintigraphic pattern is consistent with a severe impairment of peripheral lymphatic transport, of the type that would be seen, for example, in hypoplasia or aplasia of the initial lymphatics

tion in patients who develop edematous lower extremities, particularly in situations where the need for effective wound healing is heightened. The salutary response to therapy in our series of patients provides a rationale for an awareness of the potential clinical relationship between the two medical conditions.

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