Testicular Relapse of Acute Lymphocytic Leukemia: Usefulness of Color and Power Doppler Sonography

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Abstract

PURPOSE: To evaluate the usefulness of color and power Doppler sonography in detecting testicular relapse of leukemia.

MATERIALS and METHODS: Both gray-scale and color (power) Doppler ultrasound (US) were performed in seven patients. Two additional patients examined by gray-scale US only were included. The patients were 4 - 14 years old (mean age, 9 years). Ten testes were confirmed to have leukemic relapse, eight by pathology and two by clinical evidence.

RESULTS: Gray-scale US showed variable findings: heterogeneous hypoechogenicity (5) and homogeneous isoechochogenicity (5). In all seven patients (8 testes) who underwent both color and power Doppler US, diffuse and marked hypervascularity was demonstrated. One case showed enlarged epididymis with heterogeneous echogenicity, which was the same character as the involved testis.

CONCLUSION: Color and power Doppler US are useful methods in the identification of the testicular relapse of leukemia by demonstrating diffuse, marked hypervascularity in the proper clinical settings.

Index Words: Testis, US; Testis, neoplasms

Introduction

Although frequently present at autopsy, clinically evident testicular relapse in leukemic patients remains uncommon [1]. Still, leukemia is one of the most common tumors to metastasize to the testis. Because the testes may be the first site of extramedullary relapse and usually precedes hematologic relapse, early detection and prompt therapy are of the utmost importance [2,3].

The findings of testicular leukemic infiltration on gray-scale US have been nonspecific [2,4]. With the development of color Doppler US, the testicular relapse of leukemia can be more conspicuous [4,5]. Previous investigators have emphasized the relationship between the size of the testicular tumor and its vascularity, noting that small tumors (< 1.6 cm) are typical-
ly hypovascular [6]. However, small round cell infiltrations of leukemia or lymphoma were hypervascular regardless of the size [4]. Reported cases about testicular relapse of leukemia using color Doppler US were few [4]. Accordingly, because the testes may be the first site of leukemia relapse, the purpose of this study is to evaluate the usefulness of color and power Doppler US in leukemic patients with testicular enlargement for early detection and adequate treatment.

**Materials and Methods**

We investigated seven patients who underwent both gray-scale and color (power) Doppler US, as well as two patients examined by only gray-scale US. Seven patients who underwent both gray-scale and color (power) Doppler US were evaluated prospectively, and two patients who did not have Doppler study were reviewed retrospectively. The reason for including two patients who did not have Doppler study in this study is to review the variable findings of gray-scale US in testicular relapse of leukemia. We analyzed 10 testes which were confirmed to have leukemic relapse among 18 testes of 9 patients. One patient had had a relapsed testis after eight months of contralateral testicular relapse. The diagnosis of testicular relapse of leukemia was established by biopsy or orchiectomy in eight testes and by compelling clinical evidence of bone marrow relapse and follow up US after chemotherapy in two testes. One case which was confirmed by compelling clinical evidence had bilateral involvement after an eight-month interval. The patients were 4 - 14 years old (mean age, 9 years). All the patients had been previously diagnosed as acute lymphocytic leukemia (ALL). All patients complained of painless testicular enlargement without fever or tenderness.

The patients who underwent only gray-scale image were scanned with a 7.5 MHz linear array transducer on an Aloka SSD 2000 (Mure, Mitaka, Tokyo). Seven patients who underwent both gray-scale and color (power) Doppler image were scanned with either a 7 MHz linear array transducer on an Acuson 128XP (Mountain View, CA) or a 10 - 5 MHz linear array transducer on an ATL HDI 3000 (Bothell, WA) with color (power) Doppler imaging optimized for low-flow sensitivity. Gain settings were adjusted for each examination to maximize detection of slow blood flow just below background noise levels. In all cases, both testes were evaluated, including images of both testes together in the transverse plane.

The gray-scale images of each testis were evaluated for the general echogenicity of testis, the presence or absence of testicular nodules, and the echogenicity of nodules. Echogenicity was defined as homogeneous or heterogeneous and as iso-, hypo-, or hyperechoic. The determination of normal or abnormal echogenicity was based on a comparison with the echogenicity of the normal contralateral testis. Color and power Doppler images were assessed for the presence or absence of blood flow and the distribution of blood vessels in the

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**Fig. 1.** A 8-year-old boy with a history of ALL. 
A. Transverse gray-scale US on both testes shows marked enlarged left testis but has normal homogeneous isoechogenicity. B. Transverse color Doppler image on both testes shows marked diffuse hypervascularity of the involved left testis. Note an absence of vascularity on the normal right testis in the same color gain settings. The color Doppler application in this case showing normal echogenicity was helpful in detecting leukemic involvement.
enlarged testis and nodules. The determination of vascularity was based on a comparison with the normal contralateral testis. Hypervascularity was defined as a subjective increase in the concentration of vessels within the affected testis. In one patient with bilateral relapse, the echogenicity and hypervascularity were assessed subjectively.

Results

The results from each case of US findings in testicular relapse of the ALL are shown in the Table 1. Relapsed 10 testes were analyzed in 9 patients. Gray-scale US showed diffuse enlargement of the involved testis in all cases and variable findings. Five testes showed homogeneous isoechogenicity (Fig. 1,2). One of them had a small single nodule (Fig. 2). This nodule was isoechoic and well defined by a thin halo. Five testes showed heterogeneous hypoechogenicity throughout the entire involved testis (Fig. 3). One case showed enlarged epididymis with heterogeneous echogenicity, which was the same character as the involved testis (Fig. 3). Hydrocele, or thickening of the scrotal skin, which is suggestive of the inflammatory process, were not present in any case. There was no sonographic tenderness while scanning by transducer.

In all eight testes in seven patients who underwent color and power Doppler sonograms, markedly increased intratesticular vascularity was noted throughout the testis without preferential blood flow to the nodule.

Discussion

The testis is a “sanctuary” organ capable of harboring active leukemic cells at any stage of the disease due to the “blood / gonad barrier” which limits the concentration of chemotherapeutic agents within it [1]. This phenomenon is most commonly described in children with ALL [4]. All cases of our study had a history of ALL. The testes may be the first site of extramedullary relapse and usually precedes hematologic relapse. The testis was the first relapse site in six of 9 patients (66%)
in this study. Two of the other three were accompanied by bone marrow relapse, and one by central nervous system relapse.

The autopsy incidence of testicular infiltration in acute leukemia is in the range of 27.7% - 92% [7], although the reported incidence of clinically evident disease is about 5% - 30% [8]. According to recent investigation at our institution, testicular relapse of ALL was about 14.4% in clinical practice.

Gray-scale US findings in testicular leukemic infiltration are nonspecific [2,4]. The testis is enlarged and contains a focal or diffuse hypoechoic region that may be homogeneous or inhomogeneous. These findings are often quite subtle, especially in cases of diffuse involvement of the testis. A similar appearance may be seen with a primary testicular neoplasm, orchitis, testicular torsion, or other infiltrative disorders such as lymphoma or sarcoidosis [2]. Particularly, lymphoma has been known to have similar features with leukemia by both sonogram and pathology [4].

Color and power Doppler sonography allows simultaneous interrogation of gray-scale tissue appearance and an evaluation of blood flow. On application of color and power Doppler sonography in this study, diffuse and marked hypervascularity was evident throughout the enlarged testis without preferential blood flow to the nodule in all relapsed testes.

Pathologically, small round cells diffusely infiltrated the interstitium with compression, but not destruction, of the seminiferous tubules. Also, hyperplastic vessels were noted. This may correlate well with hypervascularity on color Doppler US.

The correlation between the vascularity of primary testicular tumors and the size of tumors has been reported [6]. Lesions greater than 1.6 cm were typically hypervascular, and those smaller than 1.6 cm were noted to be hypovascular with color Doppler imaging. Similarly, another study of testicular tumors in children revealed hypervascularity in neoplasms of at least 2 cm maximal diameter [5]. However, a recent study of testicular lymphoma and leukemia reported conspicuous hypervascularity without regard to the size or extent of the neoplasm [4]. All the cases in our study also showed diffuse and marked hypervascularity of the entire enlarged testis without regard to the presence or absence of focal nodules.

In a recent study [9], there was a statistically significant correlation between age and ability to detect intratesticular blood flow at both power and color Doppler imaging. Detection of intratesticular blood flow was inconsistent until 8 years of age with power Doppler US and until 12 years of age with color Doppler US.

Generally, power Doppler US is more sensitive than color Doppler US in the detection of intratesticular blood flow [9-11]. In this study, however, there was no problem for detecting the hypervascularity in color Doppler US.

Hypervascularity was striking in leukemic testicular
infiltration; however, inflammatory conditions such as orchitis or epididymo-orchitis have also been known to show hypervascularity. Generally, because both the epididymis and testis were enlarged and showed hypervascularity in inflammatory conditions, testicular hypervascularity without associated epididymal hypemia was thought to be more suggestive of a neoplastic process than of orchitis [12]. Recently, one case of epididymal involvement of leukemia was reported [4], and one of our cases showed epididymal involvement. Even though the color and power Doppler US can offer a good aid in identifying testicular leukemic involvement, especially when the findings are vague on gray-scale US, it is still difficult to differentiate between testicular leukemia and an inflammatory condition. However, clinical behavior of testicular leukemia is quite different from inflammatory conditions. In testicular relapse of leukemia, the chief complaints are painless and non-tender testicular enlargement without fever [12]. Painless and non-tender testicular enlargement can be easily ascertained during sonographic examination by the transducer (“negative sonographic tenderness sign”). This is the same principle of application of sonographic Murphy’s sign in acute cholecystitis. As ancillary findings, an absence of hydrocele or skin thickening of the scrotum can give an indication of a non-inflammatory condition.

In conclusion, in the proper clinical settings as mentioned above, the sensitivity of identification of the testicular relapse of leukemia may be increased by demonstrating diffuse, marked hypervascularity on color and power Doppler sonograms, especially in cases of subtle gray-scale US findings.

References

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연관성 분석 및 논의: 

1. 연구 방법

2. 연구 결과

3. 논의

4. 결론

사례:

1. 사례 1

2. 사례 2

3. 사례 3

[표] 2019년 18권 3호 183-188