

EUNUCHOIDISM

— VOICE PITCH ABNORMALITY AS AN AUTONOMOUS SYNDROME —

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Introduction

Disorders of voice can be classified as abnormality in pitch, intensity or quality of voice. In clinical cases, however, these three factors are often affected simultaneously and not easily separable from each other. In phoniatic practice, eunuchoidism is a specific clinical entity in which a pure form of pitch disorder is found as a cardinal symptom of the disease. It is well known that, in clinical cases of eunuchoidism, the patient shows (1) male hypogonadism noted in childhood, (2) absence or sparse growth of pubic and/or axillary hair (dystrichosis), and (3) high-pitched voice (Campbell and Harrison, 1970). It is also known that these abnormalities are due to pronounced reduction or even total absence of male sex hormone secretion from the testis. Etiologically, eunuchoidism is classified into two types; primary and secondary (Kumamoto, 1963). Primary eunuchoidism is due to the hypofunction of the testis itself with varying degrees of the reduction of hormone secretion; the complete absence of androgen is rather exceptional. On the other hand, secondary eunuchoidism results from pituitary dysfunction; and the total absence of androgen is very common. To differentiate these two types, measurement of the serum gonadotropic hormone is mandatory. The level of gonadotropic hormone is low in secondary eunuchoidism, whereas it is high in primary eunuchoidism. In the present paper, comparison will be made between these two types.

Clinical observations

In the present study, 35 cases of eunuchoidism were subjected to a long term follow-up study at the Voice and Speech Clinic of the Department of Otorhinolaryngology, at the University of Tokyo Hospital during the period from 1964 to 1968. All the cases were referred from the Department of Urology of the Hospital and none of the 35 cases had been treated before visiting our Clinic. It should be noted as an interesting fact that none of these cases subjectively complained of abnormality of voice when referred to our Clinic. Their age ranged from 18 to 36 at the first visit. Among these, 18 cases were diagnosed as primary eunuchoidism according to the classification mentioned above, and the other 17 were diagnosed as secondary.

Table I compares these two types in reference to degree of laryngeal development (manifested as laryngeal prominence) and develop-

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		Primary Type (17 cases)	Secondary Type (18 cases)
Development of Pubic Hair	-	4	11
	+	6	5
	++	6	2
	+++ (F)	1	0
	+++ (M)	0	0
Development of Laryngeal Promi- nence	-	8	14
	±	7	4
	+	2	0

Table I. Comparison of primary and secondary types of eunuchoidism, with reference to the development of laryngeal prominence and pubic hair. (F) indicates female type hair growth, while (M) indicates male type.

Development of Laryngeal Prominence	Development of pubic hair				
	-	+	++	+++ (F)	+++ (M)
-	13	5	4	0	0
±	2	5	4	0	0
+	0	1	0	1	0

Table II. Relationship between the development of laryngeal prominence and pubic hair.

ment of pubic hair. Judgments on the development of laryngeal prominence and pubic hair were made by inspection. As for laryngeal prominence, it was judged as (-) when there was no protrusion observed in the anterior neck of the patient in lateral view, while as (+) when there was a definite protrusion. A judgment of (±) was given when there was only a slight prominence. The development of the pubic hair was classified according to the criteria of Kumamoto (1963). The degree of the development of the

pubic hair has been known to reflect the level of androgen, which now is determinable by radioimmunoassay method but was estimated by 17 KS level in urine at the time of the present study. It is noted in Table I that there is a considerable difference between the two types, in that the majority of the secondary type show underdevelopment both in the laryngeal framework and pubic hair, whereas in the primary type there is a tendency towards a relatively better development of these two parameters.

A comparison was then made between the findings on the development of laryngeal prominence and pubic hair. As shown in Table II, it appears that laryngeal prominence is markedly underdeveloped when the pubic hair is absent.

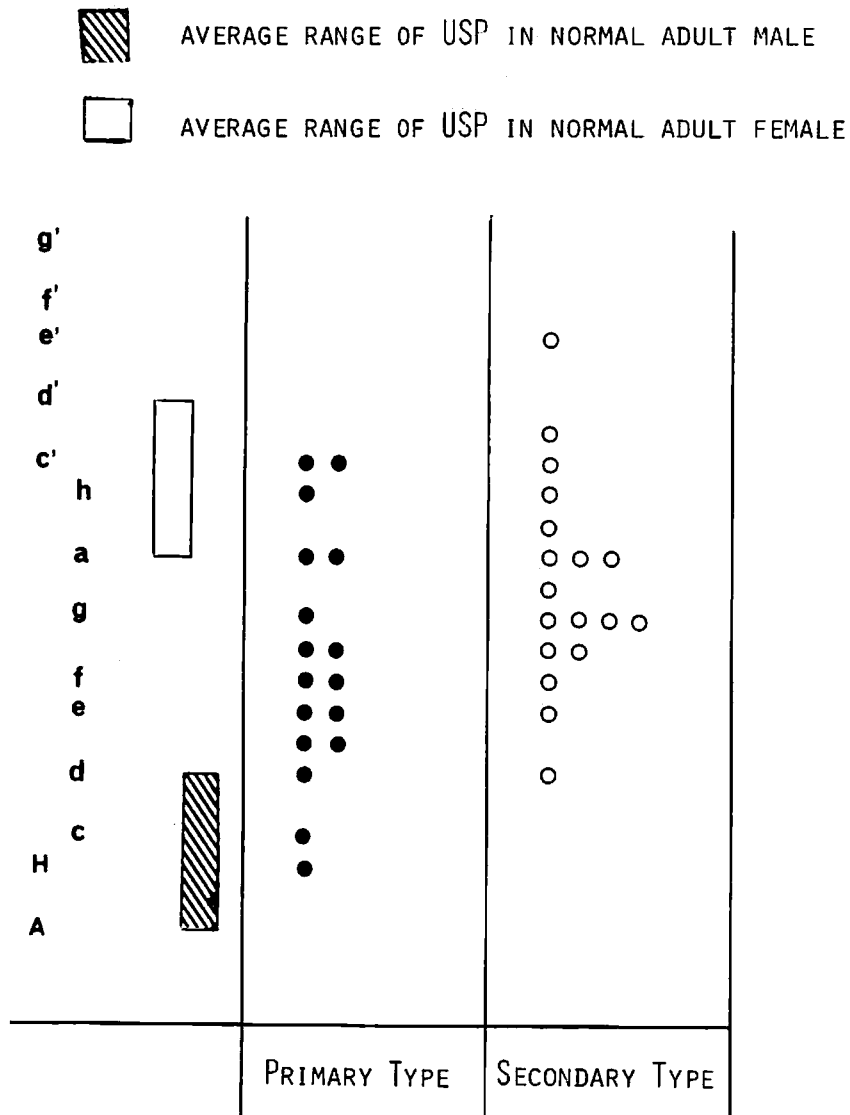


Figure 1. Usual Spoken Pitch (USP) of all the cases in the present study.

Phoniatic examination confirmed that abnormality of voice in all the cases examined was confined to abnormal pitch of voice. The voice in the these cases usually gave an acoustic impression of high-pitched and child-like characteristics. Figure 1 illustrates the distribution of the usual spoken pitch (USP) of all the cases examined. It is noted in general that their USP ranges somewhere between the average ranges of the normal adult male and female. The upper and lower limits of voice range are also plotted in Figure 2. It appears that in both types the lower limit of voice range shifts higher when compared to that of the normal male, while the distribution of the upper limit (in so-called falsetto in most cases) is more or less scattered but their average roughly corresponds to a point midway between the ranges of the normal adult male and female. These findings indicate that the pitch of their voice is comparable to that of a preadolescent boy. It also appears in Figure 1 that the pitch range tends to be somewhat higher in secondary type than in primary but the difference was found to be statistically non-significant.

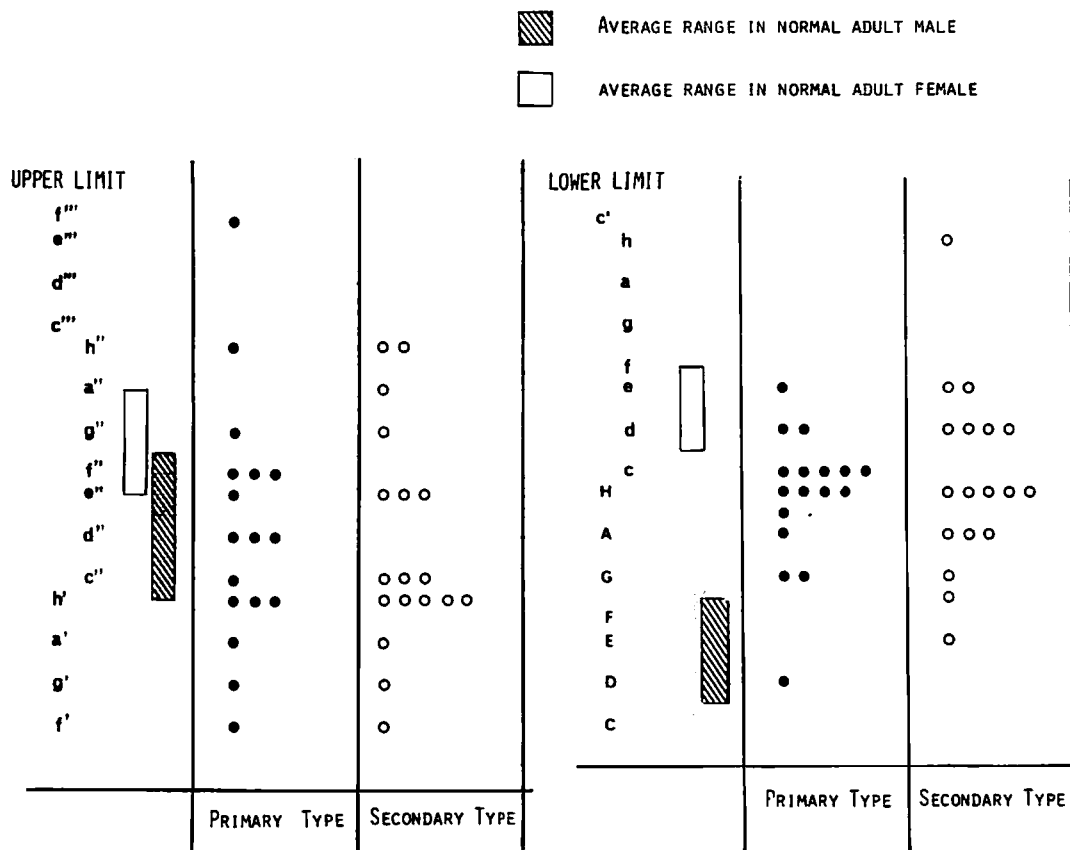


Figure 2. Upper and lower limits of voice range of all the cases in the present study.

It has been known that the level of androgen also affects the development of the bony structures. Conversely, the bone age has been known to reflect the androgen level of the subject. In order to further estimate the effect of androgen on voice pitch, the relationship between USP and the bone age of the patient was examined. Figure 3 illustrates the relationship between USP and bone age, which was judged by x-ray examination of the extremities. Although the patients in the present series were all over 18 years of age, the majority of the cases were judged under 18 years of age in their bone age. It is also noted in Figure 3 that in those subjects with the bone age of under 14, their USP was always higher than "g" and corresponded to the normal female range. In the majority of subjects whose bone age was over 15, the USP was lower than "g". These results indicate that the difference in the level of androgen which is manifested in the degree of the development of bony structures is also reflected in the difference in USP of the patients.

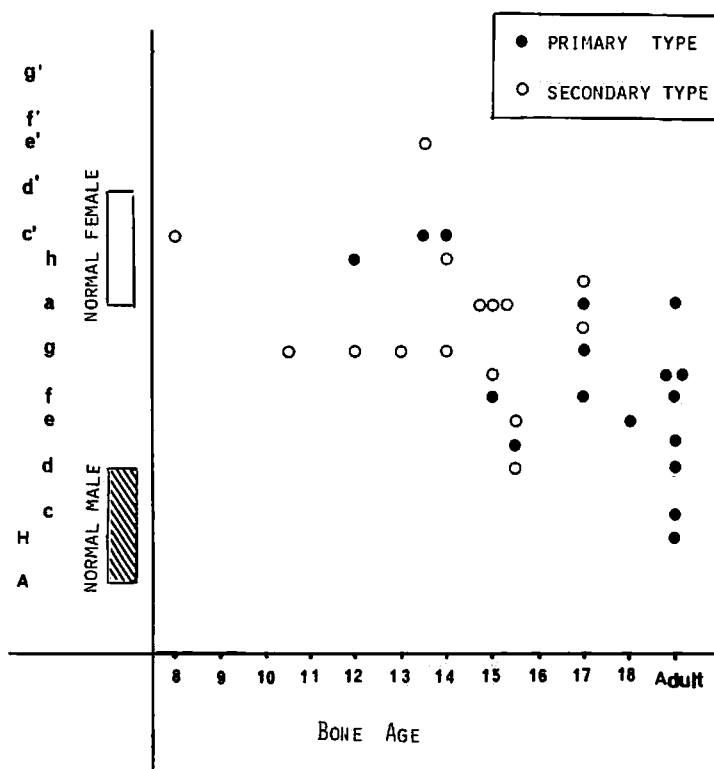


Figure 3. Relationship between USP and bone age.

An important clinical feature of eunuchoidism is that the disease can be effectively treated by male hormone preparations. In the present series, all the cases were treated with 100 mg of Depo-androgen intramuscularly every week. Figure 4 demonstrates the effect of the androgen therapy on USP. It is apparent that in most cases USP descended to the normal range

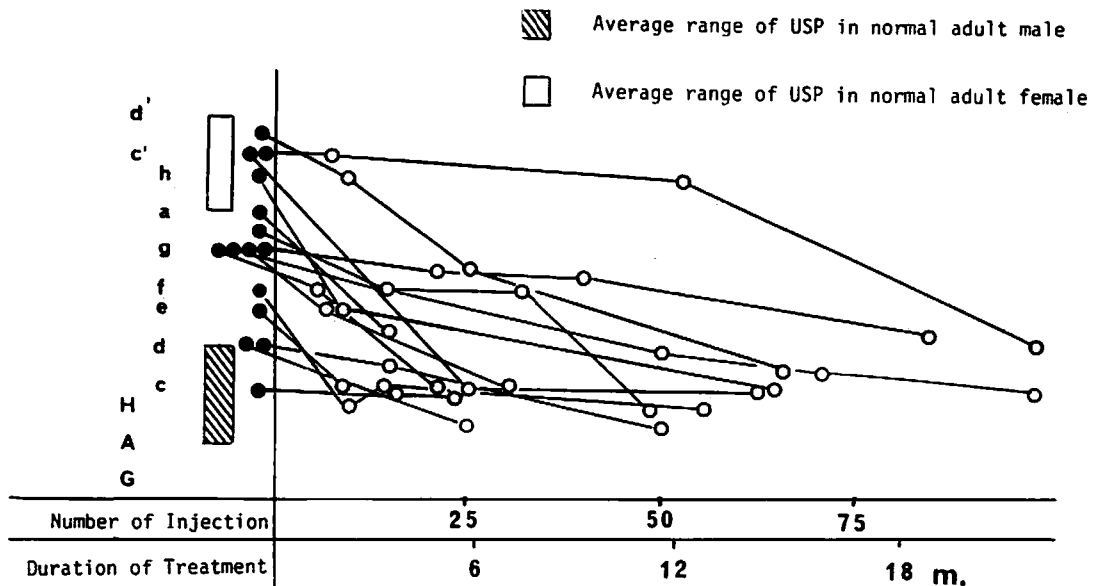


Figure 4. Time course of the change in USP as the effect of androgen treatment - Results of the follow-up.

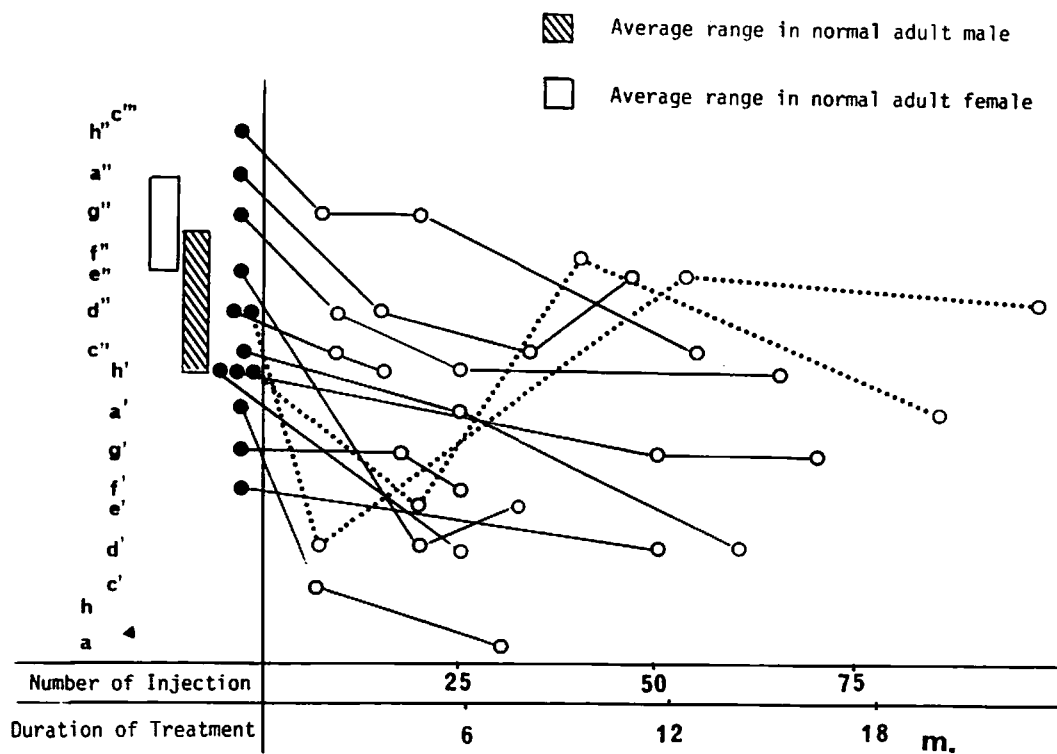


Figure 5. Time course of the change in the upper limit of voice range during androgen treatment. Dotted lines indicate those cases who became unable to phonate in head register.

within a period of from 3 to 15 months. A similar tendency was also noted in the change in the lower limit of voice range. As for the change in the upper limit of voice range, some cases became unable to phonate in falsetto for a certain period after the onset of the treatment and their upper limit of voice range abruptly descended to the level of that of the chest register as shown in Figure 5.

During the course of the treatment, laryngoscopic examinations often revealed inflammatory changes in the larynx such as diffuse hyperemia and edema and, at the same time, the so-called mutational triangle was observed at the posterior portion of the glottis. These changes are comparable to those which are not infrequently found in cases with mutational voice disorder.

As for morphological change during androgen treatment, it was found that laryngeal prominence did not necessarily develop even in those cases in which the lowering of USP was very marked (Figure 6).

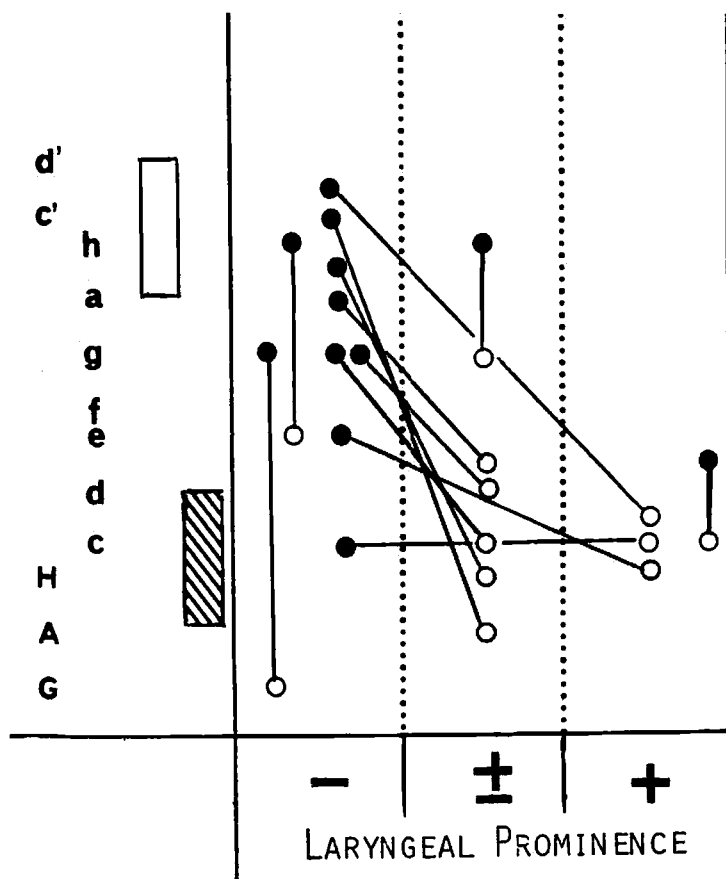


Figure 6. Relationship between the change in USP and the development of laryngeal prominence after androgen treatment.

Comments

Mutational change in voice at puberty is one of the important manifestations of the secondary sexual characteristics in the male. Sexual maturation does not occur if the secretion of the male sex hormone (androgen) from the Leydig cell in the testis is insufficient.

In the present study, it was confirmed that the level of androgen is quite important for determining the degree of sexual maturation in different parameters including the pitch of voice. It was also confirmed by long-term follow-up studies that androgen treatment was effective for lowering the pitch of voice of the patient with eunuchoidism to the normal level.

It is well worth mentioning that the clinical course of voice change during androgen treatment appears to be very gradual and often takes from 3 months to 2 years before the USP of the patient becomes comparable to that of a normal adult male. The course is certainly longer than that of normal mutation in which the lowering of USP is usually completed within a period of from 6 to 12 months. Since the amount of androgen used in the course of treatment of our cases was not much less than the estimated amount of androgen secretion at puberty in normal subjects, the apparent slow reaction to androgen treatment may also be due to abnormal receptivity of male sexual signs to androgen in these cases.

It is also interesting to note that the lowering of USP is not necessarily associated with structural changes in the laryngeal framework. Our previous study on the mutational change in voice of junior high school children revealed a similar discrepancy between the change in USP and change in laryngeal development. Namely, laryngeal development was often preceded by the change in voice (Okamura et al., 1965). This would suggest that lowering of pitch of voice at puberty or during the course of androgen treatment is primarily due to the change in the mode of laryngeal adjustments for certain structural differences which may not appear in the form of visible changes in the laryngeal framework but rather in changes in the soft tissue of the larynx. It is to be expected that the study of eunuchoidism will lead to further understanding of the mechanism of the mutation of voice in normal subjects.

Summary

Thirty five cases of eunuchoidism were subjected to laryngological and phoniatric examinations. Out of the 35 cases, 18 were diagnosed as having primary eunuchoidism and the other 17 were diagnosed as secondary. All the cases were found to have high-pitched voice and their usual spoken pitch (USP) was comparable to that of a preadolescent boy. A long term follow-up study was made on these cases with intramuscular administration of Depo-androgen every week. The treatment was found to be effective in general. The mechanism of the mutation of voice in males was discussed.

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