

ADENOMATOID TUMOR OF THE EPIDIDYMIS: A REVIEW OF JAPANESE LITERATURE

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ABSTRACT : Adenomatoid tumors are the most frequently encountered tumor of the epididymis, and forty-four cases have been reported in Japan since the first case was reported by Sakaguchi. We report the 45th case with relatively abundant leiomyomatous content, a characteristic said to be found in about 3 per cent of adenomatoid tumors. We also report the results of a review of all relevant literature published in this country.

INTRODUCTION

Primary tumors of the epididymis are relatively rare, only 107 cases^{2,3)} having been reported to date in Japan. The most frequently encountered tumor at this location is the so-called "adenomatoid tumor." The term "adenomatoid" was coined by Golden and Ash in 1945 to describe a solid benign tumor of the genital tract. Forty-four cases have been reported in this country since Sakaguchi, a Japanese physician, reported the first case in 1916¹⁾, while 160 and 310 cases have been reported abroad by Broth (1968) and Czvalinge (1972) respectively.

We wish to report one such case of the adenomatoid tumor and a review of all relevant literature.

CASE REPORT

A 47-year-old male was first seen on February 6, 1964 because of a painless mass in the right scrotum. The tail of the right epididymis was thumb-tip sized, painless, elastically firm and smooth on palpation.

Urine stain and culture for *Mycobacterium tuberculosis* were negative. A chest x-ray was non-contributory.

A right epididymectomy was performed on February 21.

Operative findings : Only a thumb-tip

sized mass with little adhesion could be found. On cut section, a soybean sized portion grayish in color was located at the center of the specimen taken from the tail of epididymis. Stain and culture for *Mycobacterium tuberculosis* from this specimen were negative. Findings in the head of the right epididymis and spermatic cord were non-contributory.

Microscopic findings : Hematoxylin-eosin stain revealed a proliferation of cells with clear cytoplasm, arranged in cord-like or, in some areas, canalicular patterns among fusiform smooth muscle fibers whose cytoplasm were eosinophilic in stain (Fig. 1). In PAS stain, these cells proved not to be eosinophilic (Fig. 2). These epithelioid cells were well stained with azocarmine according to the AZAN staining method (Fig. 3). PAP stain showed canalicular areas negative in staining which were compatible with the epithelioid cells whose arrangement was mentioned above (Fig. 4).

Diagnosis was made as adenomatoid tumor proliferation among smooth muscle fibers histologically.

STUDY OF LITERATURE

We collected and reviewed data on 44 reported cases of adenomatoid tumors in Japan (Table 1). The results were compared with western literature.

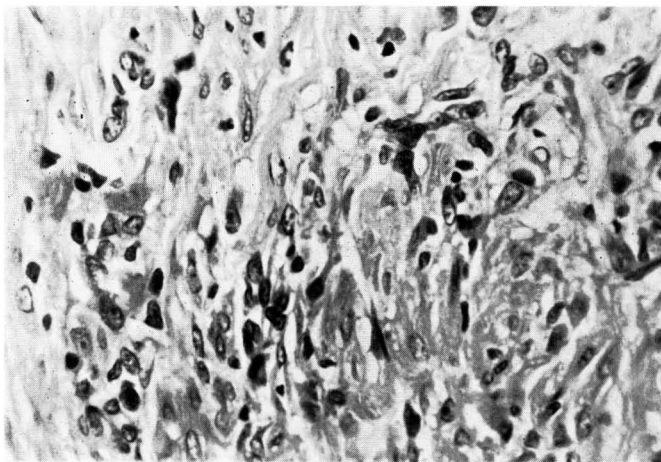


Fig. 1. Proliferation of cells with clear cytoplasm. H & E, reduced from $\times 160$.

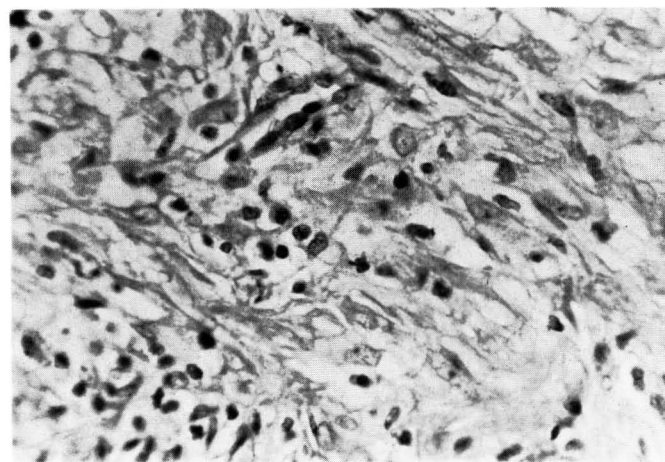


Fig. 2. Proliferating cells were not to be eosinophilic by PAS stain, reduced from $\times 160$.

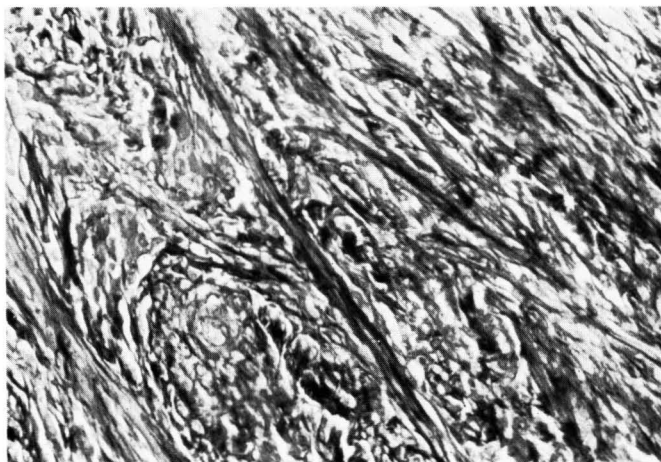


Fig. 3. Epithelioid cells stained with azocarmine. AZAN, reduced from $\times 400$.

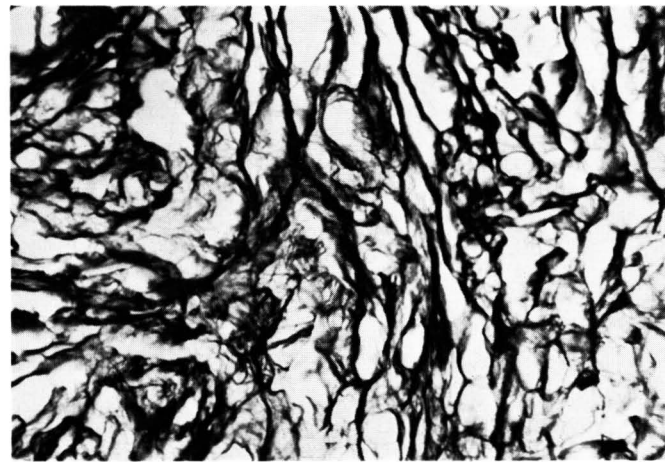


Fig. 4. Canalicular areas negative in staining. PAS, reduced from $\times 320$.

Table 1. All reported cases of the adenomatoid tumor in Japan.

Case No. & Authors	Age	Side	Size and Location (cm)	Pain	Preoperative Diagnosis	Treatment	Year
1. Sakaguchi	32		2×1.5, tail			Epididymectomy	1916
2. Harada	38	Lt.	Pea-sized, head	(-)	Epididymal tbc.	Epididymectomy	1950
3. Minami et al	47	Rt.	Little-finger-tip, tail		Epididymal tumor		1956
4. Minami et al	29	Rt.	2.5×1.8×1.5, tail		Epi. tbc.	Epididymectomy	1956
5. Momose et al	50	Lt.	Pea-sized, head	(-)	Epi. tumor	Removal of tumor	1958
6. Hironaka et al	37	Rt.	Little-finger-tip, head	(+)	Epi. tbc.		1959
7. Endo	73	Lt.	Goose-egg-sized, lt. epi.	(-)		Orchiectomy	1960
8. Sakatoku et al	35	Lt.	Finger-tip-sized, head	(-)	Epi. tbc.	Orchiectomy	1962
9. Sakatoku et al	40	Rt.	Pea-sized, tail	(-)	Epi. cyst	Epididymectomy	1962
10. Kondo et al	30	Lt.	Pigeon-egg-sized, tail	(+)	Lt. epididymitis		1962
11. Miki	30	Lt.	Pigeon-egg-sized, tail	(+)	Epididymitis	Epididymectomy	1962
12. Haneishi	1	Rt.					1962
13. Hamada	18	Lt.	Finger-tip, tail	(-)	Epi. cyst	Removal of tumor	1963
14. Sakazume et al	33	Rt.	0.9×0.7×0.7, head		Tbc. epididymitis	Removal of tumor	1963
15. Sonoda	39	Lt.	Pea-sized, tail	(+)	Epi. tbc.		1963
16. Sakurane et al	48	Lt.	Little-finger-sized, tail	(+)	Tbc. epididymitis	Epididymectomy	1963
17. Nakanishi et al	31	Lt.				Operative treatment	1964
18. Takayanagi et al	37	Lt.	Little-finger-sized, tail	(-)			1964
19. Tsuchida et al	33	Lt.	Little-finger-sized, tail	(+)	Epididymal tbc.	Epididymectomy	1964
20. Horigome et al	51	Lt.	Thumb-sized, tail				1964
21. Imamura et al	31	Lt.	Thumb-sized, tail	(-)	Epi. tbc.	Epididymectomy	1965
22. Nosaka et al	38						1966
23. Nosaka et al	48						1966
24. Oda et al	36	Lt.	Little-finger-sized, head	(+)	Epididymitis	Epididymectomy	1966
25. Yamamoto	43	Lt.	Soybean-sized, head		Epi. tbc.	Epididymectomy	1966
26. Horigome et al	57	Rt.	Little-finger-sized, tail		Epi. tumor	Epididymectomy	1967
27. Sakurane	48	Lt.		(+)			1967
28. Kikuchi et al	34	Lt.	Thumb-sized, tunica albuginea	(-)	Tbc.	Removal of tumor	1968
29. Kubo et al	36	Lt.	Little-finger-sized, head	(+)	Chr. epididymitis	Epididymectomy	1969
30. Kubo et al	31	Rt.	Little-finger-sized, head	(+)	Tbc. epididymitis	Epididymectomy	1969
31. Kondo	29	Rt.	Thumb-sized, tail & testis	(+)	Epi. tbc.	Epididymo-orchectomy	1969
32. Hiraoka et al	33	Lt.	Azuki-bean-sized, tail	(-)	Epi. tumor	Epididymectomy	1970

33. Hiraoka et al	43	Lt.	Soybean-sized, tail	(-)	Intra-scrotal tumor	Epididymectomy	1970
34. Yamamoto et al	22	Lt.	Little-finger-sized, tail		Epididymal tumor	Epididymectomy	1970
35. Seda	15	Lt.	Hen-egg-sized, spermatic cord	(+)	Hydrocele testis	Removal of tumor	1970
36. Ishikawa et al	33	Lt.	0.6×0.7×0.7, tail	(-)		Epididymectomy	1970
37. Fujita et al	54	Lt.	Little-finger-sized, tail		Undifferentiated carcinoma & squamous cell ca.	Orchiectomy	1971
38. Horigome et al	59	Lt.	Little-finger-sized, tail			Epididymectomy	1971
39. Sonoda et al	48	Rt.	Little-finger-sized, tail	(-)	Tbc. epididymitis	Operative treatment	1971
40. Hamada et al	32	Lt.	Thumb-sized, head		Epi. tumor	Removal of tumor	1972
41. Oya	31	Lt.	Thumb-sized, tail	(+)	Tbc. epididymitis	Epididymectomy	1972
42. Ota et al	54	Lt.	5cm, tail	(-)		Epididymectomy	1972
43. Kudo et al	53	Rt.	Little-finger-sized, head	(-)	Epi. tumor	Orchiectomy	1972
44. Kanda	30	Rt.	2.5×2×2, tail	(+)	Epi. tumor	Epididymectomy	1974
45. Yazaki et al	47	Rt.	Thumb-sized, tail	(-)	Tbc. epididymitis	Epididymectomy	1975

Frequency among epididymal tumors: Of 107 cases of epididymal tumors which have been reported to date in Japan, 40 cases (37 per cent) were adenomatoid tumors, the most common tumor of all. According to Mostofi, they represent 32 per cent of all tumors involving the epididymis.

Incidence: No report of the rate of incidence among the population has been prepared in Japan.

Lee et al. collected data in 1950 on 17 cases found from 800,000 patients admitted to Mayo Clinic in the 40 years from 1910 to 1949. The rate of incidence was calculated to be 1 in 47,000, while Flickinger in 1960 found 4 cases from 150,000 patients admitted to Kennedy Hospital in Memphis, Tennessee during the preceding 13 years. Frequency was presumed to be 1 in 37,000.

Age: Range in age was from 1 to 73 years. The most frequent occurrence is noted in the fourth decade. The mean age is 38 years.

Age distribution, according to Mostofi et al.⁴⁾, is from 18 to 79 years; the tumors occurred most often during the third, fourth and fifth decades. Mean age at the time of surgery was about 36 years.

Side of involvement: Twenty-nine cases (64 per cent) occurred on the left, 13

cases (29 per cent) on the right, and 3 cases (7 per cent) were uncertain because of no description concerning the side of occurrence. A right-sided preponderance was found.

Lee et al. found 58 per cent of the tumors on the right and 42 per cent on the left, while Jackson found 56 per cent on the right and 44 per cent on the left. Bilateral involvement has been reported (Norin), but is very rare. No such cases have been reported in Japan.

Location of occurrence: Twenty-five cases (56 per cent) were found at the tail of the epididymis, and 11 cases (27 per cent) at the head. One case was found at the tail and testis. One case was described only as the left epididymis. One case was at the spermatic cord, and another was at the tunica albuginea. Precise locations in the epididymis were not described in 5 cases.

According to Mostofi et al., the lower pole predominates over the upper pole as a location of occurrence by a ratio of 3 to 2.

Size of tumors: Most authors in Japan have traditionally described the size of the tumors in similitudes instead of actual measurements. Most were less than thumb-tip size. The most frequent occurrence in size was approximately little-finger-tip

size.

According to Mostofi et al., adenomatoid tumors are small, ranging from 0.4 to 5.0cm. in diameter.

Pain: Fourteen cases (31 per cent) had pain in the lump, 16 cases (36 per cent) had no pain, and in the other 15 cases (33 per cent) this was not described in the literature.

Adenomatoid tumors are said to be nearly always asymptomatic. This, however, was not the case according to the articles we reviewed.

Preoperative diagnosis: No reported cases could be diagnosed accurately prior to the operative procedure. Preoperative diagnoses were as follows: tuberculosis in 15 cases (33 per cent), neoplasm in 9 cases (20 per cent) and other diagnoses in the remainder.

Malignant changes: We have not encountered malignancy of the type reported by Söderström and Liedberg, and by Fischer and Klieger.

HISTOLOGY

The following is microscopic description by Mostofi et al.: This tumor is characterized by two major elements: epithelial-like cells and fibrous stroma. Many of the tumors contain bundles of smooth muscle, amount of which is variable, and scattered collections of chronic inflammatory cells.

The epithelial cells may be arranged as solid strands or cords, often interlaced and producing a plexiform pattern; in tubular and/or glandular form, also interconnected on interlaced (glandular type); or as dilated spaces resembling those seen in lymphangioma.

The cells may be cuboidal or low columnar, or they may be flattened and endothelioid in appearance. In general, cuboidal or columnar cells predominate in the solid and glandular types, whereas the endothelioid cells predominate in the angiomatoid type.

While any one tumor may be classified by its predominant pattern (solid, glandular, or angiomatoid), all the patterns are usually found in any given tumor.

Another fairly common feature of adenomatoid tumors is the presence of vacuoles in the epithelioid cells.

The stroma ranges from loose connective tissue to dense, collagenized tissue which is sometimes focally hyalinized. Variations in the amount and character of the stroma are frequent.

Many adenomatoid tumors exhibit a prominent knob or bundle of muscle at one pole of the tumor replacing most of the stroma at that point. Some tumors have scattered bundles of smooth muscle dispersed throughout the tumor. In about 3 per cent of the tumors, smooth muscle is abundant throughout the tumor and is the dominant element. Tumors of this type have been reported as mixed lymphangioma and leiomyoma (Halpert; Malisoff and Helpert) or as adenomatoid leiomyoma (Wilson).

Some authors have classified these tumors into 3 or 4 histological types (Table 2).

Our case belongs to type II, i.e., "cell cord with slight vacuolation" classified by Sakatoku and Takahashi⁵.

HISTOGENESIS

The histogenesis of this tumor is un-

Table 2. Histological classification of the adenomatoid tumor.

Golden and Ash (1945)	Lee et al. (1950)	Sakatoku and Takahashi (1962)
solid cord-like type	plexiform type	solid cell cord type (type I)
-----	-----	cell cord with slight vacuolation (type II)
microfollicular type	-----	-----
-----	tubular type	tubular type (type III)
macrofollicular type	canalicular type	angiomatoid type (type IV)

known. Some theories concerning its origin have been postulated. Four major theories of its origin have been supported by many authors, i. e. endothelial, mesonephric (wolffian), mesothelial and müllerian. Among them, the latter two theories have been advocated with more plausible evidence, however not enough for conclusive proof (Table 3).

Following are the theories proposed by Japanese authors.

Sakaguchi¹⁾ thought that the tumor arose from the wolffian body and duct.

Sakatoku and Takahashi (1962)⁵⁾ found tumorous tissue pathologically surrounding the ductus efferentes. They postulated from their experience and a review of literature that the origin of adenomatoid tumors is in the tissue surrounding the ductus efferentes. The ductus efferentes is the embryological remnant of the mesonephric tubule. They reasoned with confidence that the tumor may have an intimate relation to the mesonephric tubule, mesonephric duct (wolffian duct) or at least to the mesenchymal tissue surrounding the mesonephric tissue. Mose (1958) ruled out the mesothelial origin by pathological comparison with the mesothelioma originating in the peritoneum.

Oya supports the müllerian tube origin theory from the histological study in which human embryos and the specimen of the appendix of the testis taken from 31-year-old man were used.

Through their experience and a review of literature, Kubo and Murata (1969) supposed the presence of two types of adenomatoid tumors, that is, some develop from the mesonephric tissue of the epididymis and lack mesothelial characteristics with frequent continuity with the epididymal tissue, and others retain strong mesothelial characteristics without any continuity with the epididymal tissue and develop from the mesothelium of mesonephric tissue through differentiation.

Nosaka, Yamori, Morisawa and Hazama (1966) confirmed that the substance in the vacuoles of epithelial-like cells is mucopolysaccharide by using the histochemical

Table 3. Theories of histogenesis and their advocates.

Endothelial origin

- 1) Leighton (1912)
- 2) Rigano-Irrera (1925)
- 3) Marcandier and Thomas (1930)
- 4) Nicod (1934)
- 5) Scalfi (1936)
- 6) Charache (1939)
- 7) Halpert (1941)
- 8) Malisoff and Helpert (1943)
- 9) Morehead (1946)
- 10) Bolche (1952)

Mesonephric (wolffian body and duct) origin

- 1) Naegeli (1912)
- 2) Sakaguchi (1916)
- 3) Blumer and Edwards (1941)
- 4) Gordon (1941)
- 5) Codnere and Flynn (1946)
- 6) Falconer (1947)
- 7) Ragins and Crane (1948)
- 8) Longo et al (1951)
- 9) Teilum (1954)
- 10) Sakatoku (1962)

Mesothelial origin

- 1) Masson et al (1942)
- 2) Evans (1943)
- 3) Fajers (1949)
- 4) Lee et al (1950)
- 5) Ambrose (1953)
- 6) Mylius (1953)
- 7) Stavrides (1960)
- 8) Hertig (1961)
- 9) Nonaka (1964)
- 10) Broth (1968)
- 11) Abell (1968)
- 12) Kubo (1969)
- 13) Mackay (1971)

Müllerian origin

- 1) Leach (1950)
- 2) Sundarasivarao (1953)
- 3) Willis (1955)
- 4) Rankin (1956)
- 5) Jackson (1958)
- 6) Flickinger (1960)
- 7) Tsuchida (1964)
- 8) Steger (1965)

method. Considering the presence of mucopolysaccharide, the morphological resemblance to the mesothelioma and the

continuity of the tumor with the serosal cavity proved by Evans, they did not discard the mesothelial theory. They, however, supported at the same time the müllerian duct theory which accounts most clearly for the site of origin. They adopted and combined the two theories, reasoning that the tumor may originate in müllerian duct vestiges whose mesothelial characteristics have not been completely lost.

Fujita, Nakauchi, Matsumoto and Seto (1971) supported a theory similar to the one proposed by Nosaka et al.

We cannot say from our experience with any confidence which theory is most plausible. From a review of the literature, however, we are inclined to support a theory similar to Nosaka's. Adenomatoid elements might arise from the epithelioid component in the müllerian tissue, and myogenic elements from the mesenchymal component in the same tissue. Hamartomatous change could be considered to be involved in the aberrant differentiation mentioned above.

SUMMARY

A case of a epididymal adenomatoid tumor with relatively abundant leiomyo-

matous component was reported. According to Mostofi, in about 3 per cent of the cases of adenomatoid tumors, smooth muscle is abundant throughout the tumor and is the dominant element. Data from forty-five reported cases including ours in Japan were collected and reviewed.

Some characteristics were compared with those of similar tumors in Caucasians. Theories of histogenesis proposed by the authors were mentioned. We, however, cannot support the histogenesis theories with definitive evidence.

REFERENCES

- 1) Sakaguchi, Y.: Über das Adenom des Nebenhodens. Frankf. Zschr. Path., **18**: 379, 1916.
- 2) Yakushiji, M., Sakai, Y., Noda, S. and Yamaguchi, K.: Leiomyoma of the Epididymis. Acta Urol. Jap., **19**: 881, 1973.
- 3) Kuwatsuka, H., Kanetake, H. and Takahara, I.: Two Cases of Primary Epididymal Tumor. Jap. J. Urol., **66**: 200, 1975.
- 4) Mostofi, F. K. and Price, E. B.: Atlas of Tumor Pathology, 2nd Series, p. 144, Armed Forces Institute of Pathology, Washington, D. C., 1973.
- 5) Sakatoku, J. and Takahashi, Y.: Two Cases of Adenomatoid Tumor of the Epididymis with a Discussion about the Histogenesis of this Tumor. Acta Urol. Jap., **8**: 48, 1962.

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和文抄録

副睪丸アデノマトイド腫瘍：日本語文献の概観

日本医科大学泌尿器科学教室（主任：川井 博教授）

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イド腫瘍のうち約3%の割でみられるといわれている。われわれはまた本邦において報告された全文献の概観をも報告する。