Shadow Cell Differentiation in Testicular Teratomas. A Report of Two Cases

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Summary

Two cases of adult testicular teratoma with shadow cell differentiation (SCD) similar to that seen commonly in pilomatrixoma are presented. The patients aged 21 and 27 years, and both tumors were limited to the testis. The differentiation of squamous epithelium toward shadow cells is well known in cutaneous pilomatrixoma and related lesions, some odontogenic tumors, craniopharyngeoma, and it was recently observed in several visceral carcinomas. In testicular location, SCD was so far described in benign dermoid cyst but not in teratoma, suggesting that the occurrence of shadow cells could help in differential diagnosis between these lesions. This is, however, not the case and the distinction of teratoma from dermoid cyst must be based on other morphological findings.
Key words: testis – teratoma - dermoid cyst – pilomatrixoma - shadow cell differentiation

Súhrn
Diferenciácia do tieňovitých buniek ("shadow cells") v teratómoch semenníka. Popis dvoch prípadov

Popísané sú dva prípady testikulárneho teratómu s fokálnou "shadow cell" diferenciáciou (SCD), ktorá je inak typická pre kožny pilomatrixóm. Vek pacientov bol 21 a 27 rokov a oba tumory boli limitované na testis. SCD bola doposiaľ známa v pilomatrixóme a iných kožných léziach, odontogénnych tumoroch, kraniofaryngeóme a niektorých viscerálnych adenokarcinómoch. V testis bola popísaná len v dermoidnej cyste, zatiaľčo v teratóme takéto pozorovanie chýbalo. Tento rozdiel mohol byť potenciálnou pomocou pri rozlíšení medzi dermoidnou cystou a teratómom s prevahou zrelých dermoidných štruktúr. Naše pozorovania však túto možnosť negujú a diferenciálna diagnóza medzi oboma léziami zostáva tak závislá na posúdení iných zmien (dermoidnú cystu favorizuje makroskopicky cystický vzhľad bez solídnych častí a histologicky chýbanie intratubulárnej neoplázie, atypie, mitotickej aktivity a prítomnosť nanajvýš minoritnej non-dermoidnej zložky).
Kľúčové slová: testis – teratóm – pilomatrixóm - dermoidná cysta – "shadow cell" diferenciácia

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Introduction

So called "shadow" or "ghost" cells are distinctive necrotic keratinized cells that show preserved cell shape, small empty spaces left after disappearance of the nuclei and eosinophilic cytoplasm with yellowish brown to honey colored tinge (1, 8). They were described as a diagnostic feature in pilomatrixoma and other cutaneous tumors as well as in some odontogenic tumors and craniopharyngeoma (1, 3, 6, 7, 9). In recent years, the shadow cell differentiation (SCD) was observed also in some visceral carcinomas (4, 16–18). In testicular location, it was described to date only in dermoid cyst and not in teratoma, which suggested that finding of SCD could help in differential diagnosis between teratoma and dermoid cyst. Adult teratoma is, in contrast with dermoid cyst, a fully malignant neoplasm (8, 15), and therefore this differential diagnosis is of substantial importance (7, 11, 14). Here, we present a finding of SCD in two adult teratomas of the testis. Our observations indicate that SCD is not helpful in differential diagnosis between dermoid cyst and teratoma.

Materials and Methods

Six and three routine paraffin blocks were available from two tumors, respectively. The sections were stained with hematoxylin and eosin and periodic acid Schiff (PAS) with and without diastase stains. Immunostaining was performed with antibody against placental alkaline phosphatase (PLAP; polyclonal, 1:2800, DAKO, Glostrup, Denmark) using pepsin predigestion and the avidin-biotin peroxidase complex technique. Appropriate controls were used. Clinical data were obtained from urologists of the patients.

Report of Cases

Case 1

A 21–year-old man presented with testicular mass that grew slowly for several years. A radical orchiectomy was performed and irradiation of retroperitoneal and ipsilateral pelvic lymph nodes was applied. The patient is without a recurrence three months after the surgery. **Grossly**, the 6cm tumor was circumscribed and its cut surface had fibrous and cartilaginous appearance with several 1-3 mm cysts. **Histologically**, the lesion showed features of otherwise conventional teratoma containing cartilage, fibrous, adipose and smooth muscle tissues, cylindrical epithelium of both respiratory and unclassifiable endodermal type, and numerous islands of squamous epithelium (figures 1 and 2A). The cartilage and squamous epithelium were predominant. The tissues were usually mature except for several foci of endodermal epithelium with higher periepithelial cellularity of stromal spindle cells and focal fetal appearance of the cartilage. Squamous epithelium created nests and small cysts, mostly with "common" keratinization similar to that seen in epidermoid and pilar cyst of the skin [epidermoid and trichilemmal keratinization]. Some cysts contained both squamous and cylindrical epithelium. Shadow cells were found focally within masses of keratin (figure 2) or in fibrous reactive stroma, and no spatial association between them and "viable" epithelial cells was found. However, some cysts showed epithelial buds resembling initial stage of fetal hair follicle, and rare primitive pilosebaceous units were seen as well (figure 1). The shadow cells, when lying solely in the stroma, induced fibrous tissue reaction with giant cells of foreign body type. Nuclear atypia was minimal and very rare mitotic figures were found. Angioinvasion was not present. Remnant of testicular tissue showed atrophy and focal intratubular germ cell neoplasia (ITGCN) of unclassified type (13). Testicular capsule, rete testis, epididymis and spermatic cord lacked any neoplastic structure.

Case 2

A 27-year-old male presented with tumor of the left testis. Six weeks ago, the patient underwent contralateral radical orchiectomy for seminoma that had 4cm in diameter, showed conventional histology and was limited to the testis. For the left-sided lesion a radical orchiectomy was performed as well. Subsequently, an irradiation of retroperitoneal and pelvic lymph nodes was applied and the patient is without a recurrence eight years after the surgery. **Grossly**, the tumor measured 2cm in diameter, was well circumscribed, and had fibrous and cystic appearance on its cut surface. **Histologically**, it was a mature teratoma composed of a mixture of squamous and respiratory epithelial structures, focally with smooth muscle element arranged in organoid fashion. Respiratory type epithelium contained ciliated, goblet and undifferentiated cells. Some cystic islands contained both cylindrical and squamous epithelium. Squamous epithelium showed keratinization of both epidermoid and trichilemmal type, with focal presence of groups of shadow cells among the keratin lamellas (**figure 3**). Some nests of shadow cells were located solely in the fibrous stroma, focally with a giant cell reaction. A direct continuity between shadow cells and "viable" squamous epithelium was not found. The keratinization at the surface of squamous epithelium resembled that of epidermoid as well as pilar cyst. Neither pilosebaceous units nor cutaneous glands were found. Atypia was none to minimal, and mitotic figures were not found. Near the tumor, several foci of unclassified ITGCN (**figure 4**) with typical placental alkaline phosphatase (PLAP) positivity were present in atrophic testicular tissue. Like in the first case, no angioinvasion was seen and the tumor was limited to the testis, without an involvement of the rete.

Discussion

Shadow cell differentiation (SCD) represents a traditional clue to diagnosis of pilomatrixoma, matrical carcinoma [pilomatrix carcinoma] and other cutaneous tumors with differentiation toward hair matrix (1, 9). It is typical also for

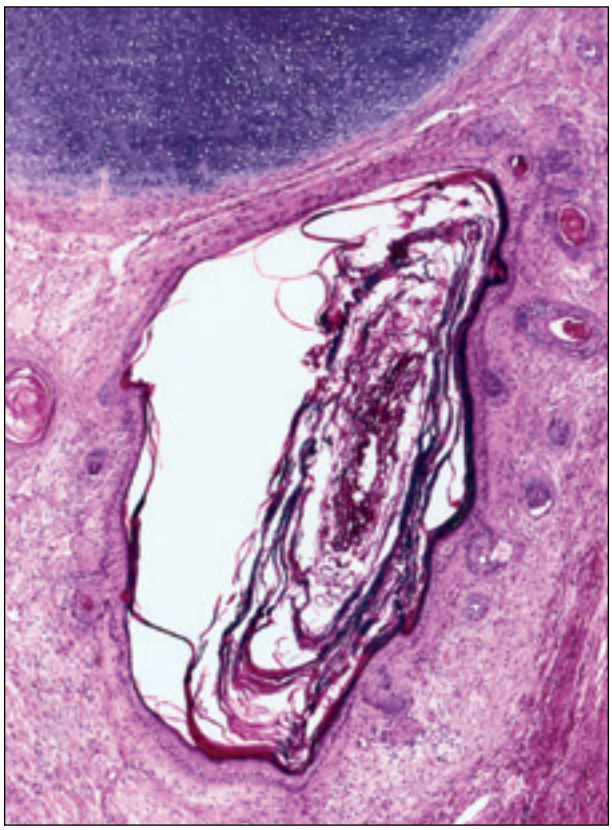
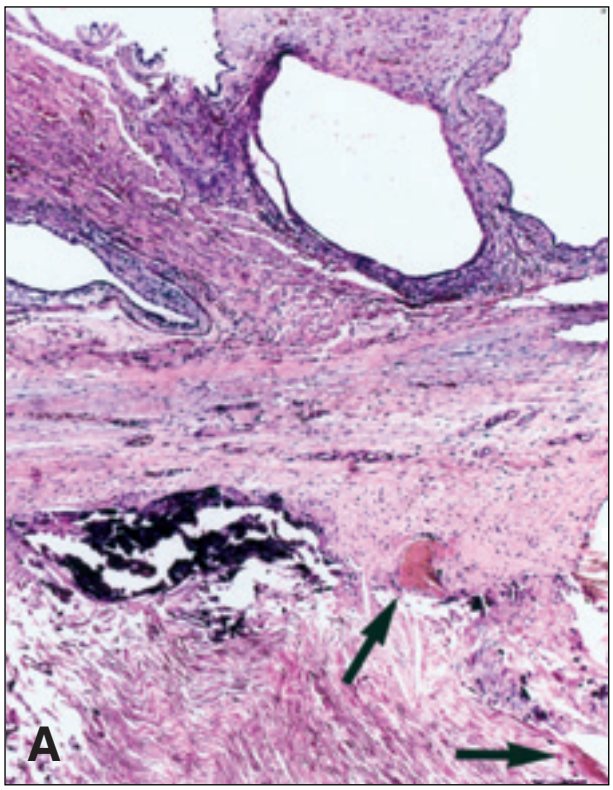


Fig. 1. Low-power view of teratoma shows epithelial, cartilaginous and fibrous structures. In the wall of the cyst primitive pilosebaceous units are seen (case 1)



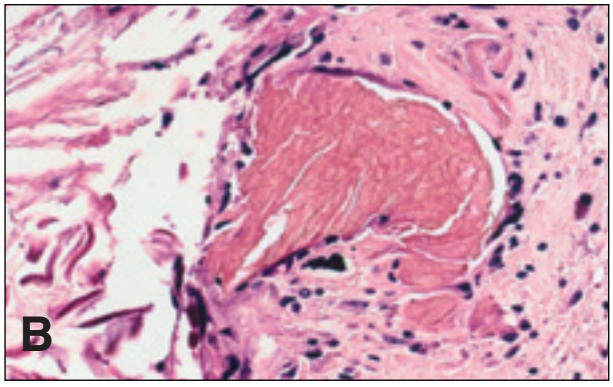


Fig. 2. Teratoma with cystic area containing keratinized cells, with focal calcification (A). Shadow cells lying among keratin lamellas are seen (arrows). High-power view (B) shows detail of shadow cell epithelium that is marked with arrows in A (case 1)

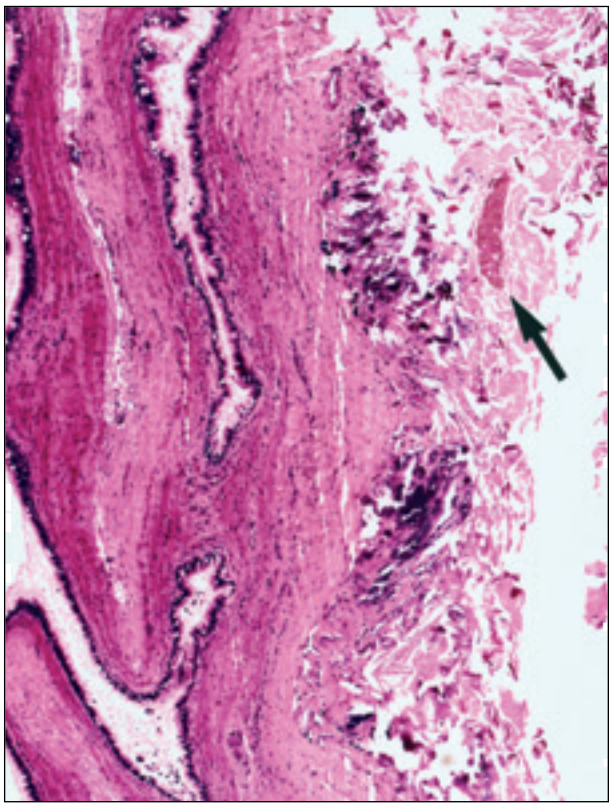


Fig. 3. Area of keratinization in mature teratoma with shadow cells lying among keratin lamellas (arrow) (case 2)

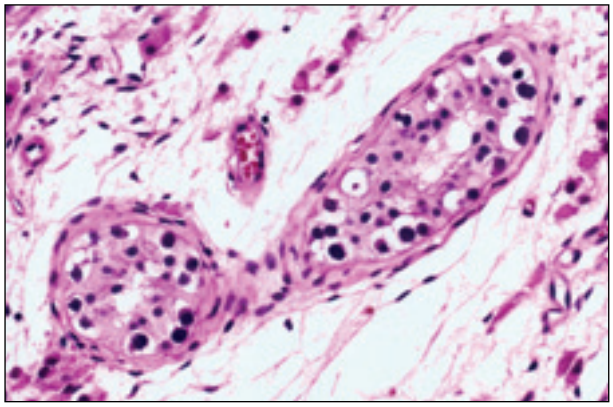


Fig. 4. ITGCN was found in testicular tissue near the teratoma in both cases (case 2)

some odontogenic lesions and for craniopharyngeoma (3, 6). In addition, shadow cells were described recently in some visceral carcinomas, endometrial hyperplasia (4, 16–18) and intracranial dermoid cyst (7) (Table 1). SCD was depicted also in recent study of prostatic squamous cell carcinomas by Parwani et al. (12). Although the authors did not specifically describe and discuss it, shadow cells are well visible in some of their figures [Figs. 1 and 8A]. Further possible tumor with SCD could be pancreatoblastoma as seen in one figure [Fig. 5b] in study by Klimstra et al. (10).

In the testis, the shadow cells were described before in two cases of benign dermoid cyst but they were not described in teratomas (11, 14). Thus, it might seem that finding of SCD could help in differential diagnosis between dermoid cyst and teratoma. This differential diagnosis is important, as dermoid cyst is invariably benign whereas adult teratoma represents a malignant neoplasm (8, 15). However, our findings of SCD in teratoma do not support this possibility, and differential diagnosis between dermoid cyst and teratoma must be based on other previously described features as follows: dermoid cysts is, in contrast with most of teratomas, a grossly cystic lesion without solid parts, it has no association with ITGCN, shows often mature hair and pilosebaceous units [sometimes hair is visible grossly], contains no more than small areas of other teratomatous elements, and lacks mitoses and significant atypia (14). We feel, however, that in rare cases application of these criteria may be misleading. Some teratomas may contain large cysts in association with only very mature structures (8) and with minimal cell proliferation and atypia [evaluation of which is quite subjective]. Further, one may suggest that there exists a possibility of synchronous occurrence of dermoid cyst and ITGCN, and in such a rare case the correct diagnosis would be extremely difficult to impossible. We think that only genetic method(s) will be diagnostic in identifying such synchronous lesions.

In cutaneous tumors, the presence of shadow cells is considered to be an indicator of hair matrix differentiation (1, 9). However, it seems that this is valid exclusively for skin lesions and not for extracutaneous ones, as in extracutaneous tumors with SCD the shadow cells are not associated with another structures of hair matrix differentiation such as smaller dark matrical cells, supramatrical cells and melanocytes or with well differentiated pilosebaceous units (1). In these extracutaneous lesions the shadow cells occurred in squamous cell areas [often in squamous morules of "adenoacanthoma"] that frequently shows also lamellar keratinization (16-18). As other signs of hair follicle differentiation are lacking, the shadow cells in these tumors represent probably only a mode of keratinization without any histogenetic relationship with hair matrix. On the contrary, the presented SCD was found in teratomas that contained skin structures and therefore the finding should be interpreted in analogy with cutaneous lesions, i.e. the shadow cells in teratoma posses probably a relationship with hair follicle differentiation, representing a result of incomplete maturation of hair matrix. Although we have found no close spatial association between shadow cells and "viable" epithelial cells, this can be result of limited sampling [the cases were found in routine files and only limited amount of blocks were available from each of the cases]. We suspect that the same was truth for both testicular pilomatrixoma-like dermoid cysts described previously (11, 14). In contrast, Hitchcock et al. (7) found shadow cells inside hair follicle in dermoid cyst of the brain, and this observation indicates that the close relationship between shadow cells and hair follicle as is known in the skin lesions applies also for well-differentiated cutaneous struc-tures in lesions outside the skin.

In conclusion, we have described SCD in teratomas of the testis. This finding indicates that in this location the presence of shadow cells is not limited to dermoid cyst, and that the differential diagnosis between dermoid cyst and teratoma should be based on other morphological features. From histogenetic point of view, we suggest that the shadow cells in teratoma that contains abundant dermoid structures ("dermoid cyst-like teratoma") indicate hair matrix differentiation the same as they do in lesions of the skin.

Table 1. Lesions with shadow cells, except for cutaneous and odontogenic tumors and craniopharyngeoma

location	histological type	reference(s)
testis	dermoid cyst, teratoma	10, 13, present cases
ovary	adenosquamous carcinoma, pilomatrixoma	2, 4
uterus	adenosquamous carcinoma, carcinosarcoma, atypical hyperplasia	16
prostate	squamous cell carcinoma	12
urinary bladder	urothelial carcinoma with squamous cell metaplasia	17
colon	adenosquamous carcinoma	16
gallbladder	small cell carcinoma with squamous cell metaplasia	18
lung	squamous cell carcinoma	5
brain	dermoid cyst	7

References

1. **Ackerman A.B., Reddy V.B., Soyer H.P.:** Neoplasms with follicular differentiation. Ardor Scribendi Publishers, 2001. – 2. **Alfsen G.C., Strom E.H.:** Pilomatrixoma of the ovary: a rare variant of mature teratoma. Histopathology 1998, 32: 182-183[L]. –3. **Bernstein M.L., Buchino J.J.:** The histologic similarity between craniopharyngioma and odontogenic lesions: a reappraisal. Oral. Surg. Oral. Med. Oral. Pathol. 1983, 56: 502-511. – 4. **Fang J., Keh P., Katz L., et al.:** Pilomatricoma-like endometrioid adenosquamous carcinoma of the ovary with neuroendocrine differentiation. Gynecol. Oncol. 1996, 61: 291-293. – 5. **Garcia-Escudero A., Navarro-Bustos G., Jurado-Escamez P., et al.:** Primary squamous cell carcinoma of the lung with pilomatricoma-like features. Histopathology 2002, 40: 201-202. – 6. **Gorlin R.J., Pindborg J.J., Redman R.S., et al.:** The calcifying odontogenic cyst. A new entity and possible analogue of the cutaneous calcifying epithelioma of Malherbe. Cancer 1964, 17: 723-729. – 7. **Hitchcock M.G., Ellington K.S., Friedman A.H., et al.:** Shadow cells in an intracranial dermoid cyst. Arch. Pathol. Lab. Med. 1995, 119: 371-373. – 8. **Jacobsen K.G., Barlebo H., Olsen J., et al.:** Testicular germ cell tumours in Denmark 1976-1980. Pathology of 1058 consecutive cases. Acta Radiol. Oncol. 1984, 23: 239-247. – 9. **Jacobson M., Ackerman A.B.:** "Shadow" cells as clues to follicular differentiation. Am. J. Dermatopathol. 1987, 9: 51-57. – 10. **Klimstra D.S., Wenig B.M., Adair C.F., et al.:** Pancreatoblastoma. A clinicopathologic study and review of the literature. Am. J. Surg. Pathol. 1995, 19: 1371-1389. – 11. **Minkowitz G., Lee M., Minkowitz S.:** Pilomatricoma of the testicle. An ossifying testicular tumor with hair matrix differentiation. Arch. Pathol. Lab. Med. 1995, 119: 96-99. – 12. **Parwani A.V., Kronz J.D., Genega E.M., et al.:** Prostate carcinoma with squamous differentiation: an analysis of 33 cases. Am. J. Surg. Pathol. 2004, 28: 651-657. – 13. **Skakkebaek N.E**.: Possible carcinoma-in-situ of the testis. Lancet 1972; 2: 516-517. – 14. **Ulbright T.M., Srigley J.R.:** Dermoid cyst of the testis: a study of five postpubertal cases, including a pilomatrixoma-like variant, with evidence supporting its separate classification from mature testicular teratoma. Am. J. Surg. Pathol. 2001, 25: 788-793. – 15. **Ulbright T.M.:** Gonadal teratomas: a review and speculation. Adv. Anat. Pathol. 2004, 11: 10-23. – 16. **Zamecnik M., Michal M.:** Shadow cell differentiation in tumours of the colon and uterus. Zentralbl. Pathol. 1995, 140: 421-426. – 17. **Zamecnik M., Michal M., Mukensnabl P.:** Shadow cells in extracutaneous locations. Arch. Pathol. Lab. Med. 1996, 120: 426-428 [L]. – 18. **Zamecnik M., Michal M., Mukensnabl P.:** Pilomatrixoma-like visceral carcinomas. Histopathology 1998, 33: 395[L].

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