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ORIGINAL ARTICLE

Seminal Tract Amyloidosis: Synchronous Amyloidosis of the Seminal Vesicles, Deferent Ducts and Ejaculatory Ducts

Lea Rath-Wolfson[1,2] · **Golan Bubis**[3] · **Shmuel Shtrasburg**[4] · **Asaf Shvero**[5] · **Rumelia Koren**[1,2]

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Abstract Senile Seminal Vesicle Amyloidosis (SSVA) increases with age. Involvement of the whole seminal tract, i.e. the seminal vesicles, ejaculatory and deferent ducts was first reported by us in the International Symposium on Amyloidosis 1998. Since then we encountered four more cases of SSVA. In all these cases the ejaculatory and deferent ducts were also involved by amyloid. The amyloid was located mostly sub-epithelially, stained positively with Congo red, gave green birefringence under polarized light and was permanganate sensitive, slightly positive for lactoferrin immunostaining and negative for all known amyloid types. In recent years the amyloid was found to be derived from Semenogelin I, a major constituent of the seminal fluid which is present in the epithelial cells of the seminal vesicle and vas deference. This would explain the deposition of amyloid not only in the seminal vesicles but also in the deferent an ejaculatory ducts which transport the seminal fluid. In a review of the literature we found three more articles on SSVA in which the amyloid was not limited to the seminal vesicles alone. We propose to designate this type of amyloid as "Senile seminal *Tract* Amyloidosis" (SSTA) instead of "Senile Seminal *Vesicle* Amyloidosis (SSVA)".

Keywords Senile seminal vesicle amyloidosis (SSVA) · Ejaculatory duct amyloidosis · Spermatic duct amyloidosis · Senile seminal tract amyloidosis (SSTA)

Introduction

Senile Seminal Vesicle Amyloidosis (SSVA) is one of the organ-limited amyloidosis, which has attracted little attention. In a search of PubMed we found only 50 articles on this subject. This amyloid has unique histochemical and immunohistochemical properties not shared with other amyloid types. Like amyloid AA it is sensitive to permanganate pretreatment but it lacks tryptophan [1]. The amyloid deposits are usually asymptomatic, however, some cases of SSVA presented with hematospermia [2–6], which resolved spontaneously in an average of 14 months. Some cases of SSVA have been misinterpreted on MRI as invasion by prostatic or urinary bladder carcinoma [7–9], and in several cases it simulated primary tumors of the seminal vesicle [10]. We therefore feel that the awareness of SSVA is important.

In the International Symposium on amyloidosis, 1998, we presented the first case of synchronous amyloidosis of the seminal vesicles, deferent ducts and ejaculatory ducts [11], since then we encountered four more cases of SSVA. In view of our previous experience we stained the deferent ducts and the ejaculatory ducts with Congo-red. In all five cases these structures were also involved by amyloid. We therefore propose to designate this condition as Senile *Seminal Tract* Amyloidosis (SSTA), instead of Senile Seminal *Vesicle* Amyloidosis.

✉ Golan Bubis
bubisgolan@gmail.com

[1] Department of Pathology Hasharon Hospital, Petah-Tiqva, Israel

[2] Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

[3] Medicine Program, St. George's University of London, University of Nicosia, 93 Agiou Nikolau Street, Egnomi 2408 Nicosia, Cyprus

[4] Heller Institute of Medical Research, Sheba Medical Center, Tel-Hashomer, Israel

[5] Department of Urology, Sheba Medical Center, Tel-Hashomer, Israel

Material and Methods

Patients

Five male patients aged 58–82 were investigated. Two had prostatic carcinoma and underwent total prostatectomy. Two patients underwent supra-pubic prostatectomy for prostatic hyperplasia; however, due to anatomical site problems the seminal vesicles were included in the surgical specimen as well. One patient underwent Miles operation for carcinoma of the rectum and prostatectomy was performed due to adherence of the rectum to the prostate.

Pathological Examination

The specimens were examined and processed as described by us previously [12]. By this method all the prostate, the ejaculatory and deferent ducts as well as the seminal vesicles were available for histological examination. The specimens were processed routinely, embedded in paraffin and stained with Hematoxylin and Eosin. (H&E)

Histochemical Stain

The sections were stained with Congo red (CR) with and without permanganate pretreatment, and inspected under bright and polarized light using a Leitz microscope with tension free optics [13].

Immunohistochemical Stains

Sections containing amyloid were stained immunohistochemically for lactoferrin and with a panel of antibodies specific for the five major amyloid fibril proteins [Anti: AA, Aλ, Aκ, β2M and AF (TTR)]. The paraffin blocks containing amyloid were also examined by the Shtrasburg method [14].

Results

In all five cases histological examination revealed large deposits of amyloid in the three components of the seminal tract. It stained with Congo red and gave green birefringence under polarized light which was abolished after permanganate pretreatment. Figure 1 shows the ejaculatory ducts with amyloid located sub-epithelially. Figure 2 shows the seminal vesicle stained by congo- red and showed green birefringence under polarized light. The amyloid was permanganate sensitive i.e. the CR staining was completely abolished after permanganate pretreatment. It did not show any protein band by the Shtrasburg method which identifies amyloid A by SDS electrophoresis [14].

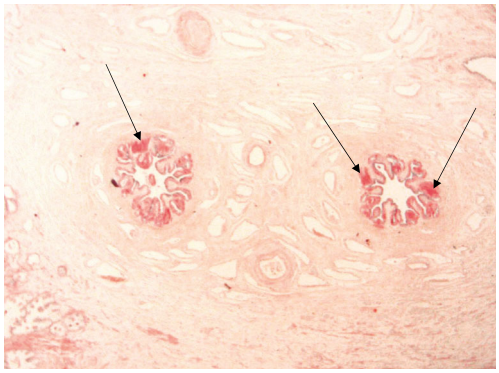

Fig. 1 The two ejaculatory ducts embedded in the prostate. Note the subepithelial amyloid deposits (*arrows*). CR X 10

Immunohistochemically the amyloidal was slightly reactive to lactoferrin and non-reactive to immunostains with Anti: AA, Aλ, Aκ, β2M and AF (TTR). The corpora amylacea found in the prostate were positive for β2M.

Discussion

Senile Seminal Vesicle Amyloidosis (SSVA) has usually been reported as an incidental finding in autopsy material, total prostatectomy and prostatic needle biopsies.

Incidence The incidence increases with age. Table 1 shows some of the SSVA series from the literature. Unger et al. [15] found 6 cases of SSVA out of 200 radical prostatectomies. Erbesdobler et al. [16] found 73 cases out of 6575 and Argon et al. [17] found 10 cases out of 207 radical prostatectomies. Kee et al. [18] found 21 out of 447 prostatectomy specimens with a higher incidence in the Korean patients than in US patients, and higher incidence with age. In a post mortem series the incidence is usually higher and increases with age. Pitkänen et al. [1] found 34 cases of SSVA out of 209 autopsies with an incidence of 21% in patients aged over 75 years old. SSVA is also found incidentally in prostatic needle biopsies. Yang et al. found 7 cases out

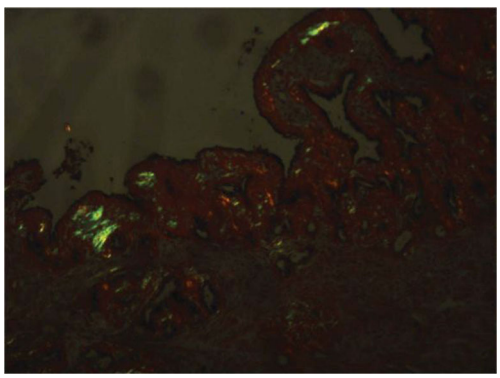

Fig. 2 The seminal vesicle shows subepithelial birefringent apple green amyloig. CR X 10 seen under crossed polars

Table 1 Some of the series of SSVA reported in the literature and the anatomic sites involved

Author/Reff	Year	No. of Cases	Anatomic Sites involved
Goldman H [20]	1963	3	SV + DEF
Pitkänen et al. [1]	1983	34/209	SV
Unger et al. [15]	1997	6/200	SV
Koren et al. [11]	1998	1	SV + DEF + EJ
Jun et al. [7]	2003	2	SV + DEF
Kee et al. [18]	2008	21/447	SV + DEF + EJ
Erbersdobler et al. [16]	2009	73/6575	SV
Argon et al. [17]	2012	10/207	SV
Present article	2016	4	SV + DEF + EJ

SV Seminal vesicle, *DEF* Deferens duct, *EJ* ejaculatory ducts

of 1500 biopsies. They concluded that routine investigations for systemic amyloidosis is not warranted [19].

Chemical Type of the Amyloid Like Amyloid AA and unlike all other known amyloid types, potassium permanganate pretreatment abolished the CR staining. All the immunohistochemical stains for amyloid AA, Aλ, Aκ, β2M were negative in our cases and in those of the literature as well. The chemical nature of SSVA has been investigated by several researchers. As lactoferrin is secreted by the seminal vesicle [21], some researches [22, 23] suggested that lactoferrin was a constituent in localized SSVA as the amyloid substance was immunoreactive for lactoferrin.

Cornwell et al. [24] reported that the amyloid fibrils in SSVA were composed mainly of a 14 kDa protein secreted from the epithelium of the seminal vesicle as an exocrine product. Antiserum for this protein reacted with seminal amyloid material and some normal seminal vesicle epithelial cells but it did not react with any other type of amyloid known to date.

The most recent advance in understanding the pathogenesis of SSVA was reported by Linke et al. [25] who found that the amyloid was derived from semenogelin I, which is the major secretory product of the seminal vesicle. They showed it by mass spectrometric analysis of the amyloid and by the positive immunostaining with anti-semenogelin I antibodies. They designated this form of amyloidosis as amyloid semenogelin 1 (ASgl). Sharma et al. [26] succeeded in forming amyloid-like aggregates of semenogellin1 showing detergent stability and found that the presence of Zn2+ substantially inhibits their amyloid aggregation in vitro. They proposed that possibly the high Zn2+ found in seminal plasma of young individuals may have preventive role against aggregation of semenogelin into amyloid deposits.

Lundwall et al. found intense immunostaining for semenogelin 1 and 2 in the secretory epithelium of the seminal vesicle. An equally intense staining was seen in vas deferens and the ampulla, indicating high semenogelin concentration also in secretion from the epithelium of the spermatic ducts [27].

Seminal Tract Involvement In 1963 Goldman H [20] described 3 cases of SSVA with vas deference involvement. In 1998 we described [11] the first case where the whole seminal tracts, including the ejaculatory and deferent ducts, were involved. Since then, Jun et al. [7] reported two cases of SSVA involving the vas deferens and Kee et al. [18] reported the involvement of the whole seminal tract in 21 cases. (Table 1) All the other series reported amyloid deposition in the seminal vesicles alone. However, in these reports the ejaculatory and deferent ducts were possibly not examined as these structures were not specifically mentioned in the manuscripts. Therefore we suppose that this type of amyloid involves the whole intra-pelvic seminal tract. Nevertheless this is still not generally accepted, as in the official clinical classification of the amyloidosis 2014, still the target organ of semenogelin 1 amyloid is the vesicula seminalis [28].

Conclusion

The amyloid of SSVA is deposited not only the seminal vesicles but also in the ejaculatory and deferens ducts. It is derived from semenogelin I, a major constituent of the seminal fluid and is produced by the epithelium of the seminal vesicle and vas deferens. Therefore it is self-evident that the amyloid derived from it could involve the whole seminal tract. We propose to designate this condition as Senile Seminal *Tract* Amyloidosis (SSTA) instead of Senile Seminal *Vesicle* Amyloidosis (SSVA).

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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