Case Report

A microcystic/reticular schwannoma in an unusual site: description of a retroperitoneal location and review of the literature

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Summary
Microcystic/reticular (MRV) schwannoma has been described since 2008, but remains a rarely encountered entity. MRV has a predilection for visceral locations and has variable histologic appearances. Given its rarity and anatomic variability, this entity could raise differential diagnostic issues with other tumours and malignancies.

We describe the case of a 69-year-old male followed at IRCCS Ospedale Policlinico San Martino of Genoa for his previous history of non-Hodgkin lymphoma. A para-aortic mass was discovered during follow-up, which -due to its stability, also after chemotherapy- had been hypothesized to be a non-lymphomatous lesion; given the dimensions and the site, the mass was removed. Histological evaluation showed a nodule limited by a slight fibrous capsule and characterized by a proliferation of medium-sized fusiform cells, with elongated nuclei and scarce eosinophilic cytoplasm. Given the lack of malignant signs and the strong expression of protein S-100, a diagnosis of mesenchymal neoplasia with expression of neural markers compatible with reticular schwannoma was made. The neoplasm has not recurred since its removal.

The case we present is, at our best knowledge, the first described in the retroperitoneum, a site where the exclusion of other mesenchymal malignancies is mandatory. The rarity and variability of presentations could create problems of differential diagnosis both with mucinous-producing carcinomas or with other soft tissue tumours, with myxoid or reticular structure. The description of this case could help raise information on this rare neoplasm and help distinguish it from other malignancies, especially in unusual sites.

Key words: reticular schwannoma, pathology, soft tissue tumor, rare neoplasms

Introduction
Schwannomas are benign tumors of the nerve sheath, typically solitary and with wide anatomic distribution. Morphologic variants of schwannomas include ancient, plexiform, cellular, epithelioid and melanotic 1-3. A more recently identified variant is the microcystic/reticular (MRV) schwannoma, described for the first time in 2008, and subsequently described in some case reports, although remaining a rare encountered entity 1-10.

In contrast to other variants of schwannomas, MRV has a predilection for visceral locations and it is histologically characterized by a striking microcystic and reticular growth pattern, composed of anastomosing and intersecting spindle cells admixed with vacuolated cells within a collagenous to myxoid stroma 1-2.
Due to its rarity and anatomic variability, this entity could raise differential diagnostic issues with other tumors and malignancies. We here describe a case of microcystic/reticular schwannoma, developed in the retroperitoneum of a 69-year-old male, in order to help collect other information on this tumor.

Case presentation

A 69-year-old male was followed at Ospedale Policlinico San Martino of Genoa because of his previous history of non-Hodgkin lymphoma. The evaluation of CT scans during and following chemotherapy showed a dishomogeneous para-aortic mass initially of 5 centimeters, which – due to its stability for five years, also after chemotherapy – had been hypothesized to be a non-lymphomatous lesion. Radiologically the mass was suspected to be a paraganglioma or a neuroendocrine tumor. The patient underwent the surgical excision of the mass, which macroscopically resulted to be a nodular formation of 10 cm of maximum diameter, partly covered with adipose tissue. The cut surface was dishomogeneous, yellowish, with translucent and hemorrhagic areas. Hematoxylin-eosin sections were obtained from numerous paraffin-embedded inclusion blocks and subsequent immunohistochemical reactions for S100, EMA, CD34, CD31, MDM-2, Melan-A, HMB45, Smooth Muscle Actin, Desmin, Calponin, Synaptophysin, Chromogranin, CD117, HHV-8, Ki-67 and Cytokeratins AE1-AE3 and CAM5.2 were performed (Ventana Benchmark).

Histological evaluation showed a circumscribed mass, peripherally limited by a slight fibrous capsule (Fig. 1) and characterized by a proliferation of medium-sized fusiform cells, with elongated nuclei and scarce eosinophilic cytoplasm (Fig. 2). Neoplastic elements had various pattern of growth: some areas showed a tight proliferation, while the others were more loosely arranged and showed a microcystic/reticular structure (Fig. 3).
majority of the lesion had partly a microcystic or a reticular structure, depending on the width of space between the anastomotic strands of fusiform cells (Fig. 3). Spaces between neoplastic cells were filled with focally myxoid and haemorragic content. Numerous vascular structures were mixed with neoplastic cells. No necrosis or mitotic figures were found. No aggregations of lymphocytes or other inflammatory cells were identified. Immunohistochemical evaluation highlighted a strong and diffuse expression for protein S-100 in fusiform elements (Fig. 4), with a weak reaction for EMA in the capsule. Vascular markers CD31 and CD34 were expressed in intranodular vessels. Cytokeratins (AE1-AE3 and CAM5.2) and muscular, neuroendocrine and melanocytic stainings (Smooth Muscle Actin, Desmin, Calponin, Synaptotisin, Chromogranin, CD117, MDM-2, Melan-A, HMB45 and HHV-8) were all negative. Given the lack of malignant signs and the strong expression of protein S-100, a diagnosis of mesenchymal neoplasia with expression of neural markers compatible with reticular schwannoma was made.

Discussion

Schwannomas are benign tumors of the nerve sheath, typically solitary and with wide anatomic distribution, usually arising in the fourth or fifth decade of life, in the subcutaneous tissue of distal extremities, or in the head and neck region of adult patients, with no gender predilection.

Among the numerous possible variants of this tumor, in 2008 Liegl et al. first described the microcystic/reticular schwannoma. This variant has a predilection for visceral locations, especially gastrointestinal tract, and a slight predilection for women, with a wide age range distribution. Histologically it is usually characterized by a striking microcystic and reticular growth pattern, formed by anastomosing and intersecting spindle cells admixed with vacuolated cells within a collagenous to myxoid stroma; scattered Verocay bodies are evident. Tumor cells have spindle to vacuolated shape and ovoid nuclei, inconspicuous nucleoli, and eosinophilic cytoplasm. Foci of classical schwannoma patterns (Antoni A and Antoni B areas) are often present. Scattered inflammatory cells could be present, but lymphoid aggregates are rare. Nuclear atypia, necrosis, and mitotic activity are rare or absent.

Since 2008, a total of 36 cases have been described, all confirming the benign nature of the lesion and showing the variability of possible presentations. The majority of cases arose in the gastrointestinal tract, both upper and lower segments, but subcutaneous fat and glandular organs could be affected by the neoplasia. Soft tissue localizations have been described in subcutaneous fat of arms, legs or back, but no cases has yet been described in deep soft tissue. Rarely, microcystic/reticular schwannoma had been described also in brain tissue, spinal cord and in the head and neck region (Tab. I).

The rarity and variability of presentations could create problems of differential diagnosis both with mucinous-producing carcinomas (especially on small biopsies) or with other soft tissue tumors, with myxoid or reticular structure. In the current case, the site of presentation (retroperitoneal tissue) and the lack of a diffuse myxoid stroma helped us excluding malignant soft tissue neoplasms as myxoid liposarcoma and myxofibrosarcoma, both usually with a superficial origin (mainly thigh and extremities). Morphology, with the absence of lipoblast-like elements and lacking of “chicken-wire” vessels, and MDM-2 negativity ruled out also the possibility of a dedifferentiated liposarcoma of retroperitoneum. The intense staining with S100 and the peripheral weaker staining for EMA made us think about a nervous origin of the tumor.

Reticular perineuroma, another possibility based on morphology, usually contains slender, elongated spindle cells with bipolar cytoplasmic processes highlighted by EMA staining, and tumor cells are negative for both S-100 protein and GFAP; our case showed an opposite phenotype (EMA negative, S100+ and GFAP+).
The possibility of a carcinoma with mucinous production and melanoma were both excluded on morphology and with immunohistochemical reactions. The most striking feature of our case was the high number of vascular structures admixed with spindle cells: stainings with CD31 and CD34 helped us to demonstrate a non-hyalinized wall and a regular course of vessels, without an alteration in their structure. This let us excluded also vascular neoplasms, such as hemangioma or angiosarcoma.

Table I. Sites and characteristics of all described cases.

| Case no. | Age/sex | Site                  | Growth            | Reference          |
|---------|---------|-----------------------|-------------------|--------------------|
| 1       | 39/F    | Esophagus             | Unencapsulated    | Gu et al.         |
| 2       | 72/F    | Stomach               | Unencapsulated    | Liegl et al.      |
| 3       | 63/F    | Stomach               | Unencapsulated    | Chetty et al.     |
| 4       | 67/F    | Mid-jejunum           | Unavailable       | Agaimy et al.     |
| 5       | 93/F    | Jejunum               | Unencapsulated    | Liegl et al.      |
| 6       | 78/M    | Small intestine       | Focal infiltration| Liegl et al.      |
| 7       | 43/F    | Meso-appendix         | Encapsulated      | Tang et al.       |
| 8       | 68/M    | Cecum                 | Focal infiltration| Liegl et al.      |
| 9       | 67/F    | Cecum                 | Focal infiltration| Agaimy et al.     |
| 10      | 32/F    | Ascending colon       | Focal infiltration| Lee et al.        |
| 11      | 70/F    | Sigmoid colon         | Unencapsulated    | Kienemund et al.  |
| 12      | 70/F    | Sigmoid colon         | Unavailable       | Kienemund et al.  |
| 13      | 61/M    | Sigmoid colon         | Unencapsulated    | Trivedi et al.    |
| 14      | 73/F    | Rectum                | Unencapsulated    | Liegl et al.      |
| 15      | 50/F    | Right arm             | Encapsulated      | Liegl et al.      |
| 16      | 55/M    | Right forearm         | Encapsulated      | Chaurasia et al.  |
| 17      | 30/F    | Upper arm             | Partially encapsulated | Luzar et al.     |
| 18      | 55/M    | Right upper arm       | Partially encapsulated | Luzar et al.     |
| 19      | 56/F    | Back                  | Encapsulated      | Liegl et al.      |
| 20      | 11/M    | Upper back            | Unencapsulated    | Liegl et al.      |
| 21      | 28/M    | Back                  | Partially encapsulated | Luzar et al.     |
| 22      | 26/M    | Left masticator space | Unencapsulated    | Lau et al.        |
| 23      | 69/M    | Retroperitoneum        | Encapsulated      | Our case          |
| 24      | 62/M    | Pancreas              | Unencapsulated    | Liegl et al.      |
| 25      | 41/M    | Pancreas              | Unencapsulated    | Shen et al.       |
| 26      | 53/M    | Left adrenal gland    | Focal infiltration| Liegl et al.      |
| 27      | 31/F    | Adrenal gland         | Encapsulated      | Zhou et al.       |
| 28      | 60/M    | Adrenal gland         | Unencapsulated    | Xie et al.        |
| 29      | 59/F    | Parotid gland         | Unencapsulated    | Pang et al.       |
| 30      | 34/M    | Submandibular gland   | Unencapsulated    | Lau et al.        |
| 31      | 76/F    | Bronchus              | Unencapsulated    | Liegl et al.      |
| 32      | 22/F    | Frontal lobe          | Unencapsulated    | Pearson et al.    |
| 33      | 61/F    | Right mandible        | Focal infiltration| Yin et al.        |
| 34      | 28/M    | Right neck            | Encapsulated      | Gong et al.       |
| 35      | 22/F    | Palate                | Encapsulated      | Guo et al.        |
| 36      | 35/M    | Cervical spine        | Unencapsulated    | Li et al.         |
| 37      | 40/M    | Lumbar spinal canal   | Encapsulated      | Liu et al.        |
Conclusions

The case we present is, to the best of our knowledge, the first described in the retroperitoneum, a site where the exclusion of other mesenchymal malignancies is mandatory, united with, in the specific patient, the exclusion of a lymphoproliferative disorder. We hope that this description will help add information about this rare and unusual neoplasm.

CONFLICT OF INTEREST

The Authors declare no conflict of interest.

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ETHICAL CONSIDERATION

Neither patient consent nor ethical approval was sought: all patients attending San Martino Hospital are informed about the use of their data for continuing research at the Hospital.

AUTHORS’ CONTRIBUTION

RB, GG: conception, data collection, drafting and final review. GFO, JLR: review and corrections. BS, VGV: drafting and final corrections.

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