Retroperitoneal malignant schwannoma

A case report

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Summary

This is the 15th fully documented case of retroperitoneal malignant schwannoma in the English-language literature. The histogenesis and morphological features are described. Apart from recommending radical surgical resection with adequate tumour margins, the literature provides very little guidance on management. Our patient received Adriamycin and dacarbazine as adjuvant therapy and is clinically without evidence of disease 6 months after definitive surgery.


Malignant schwannoma is a primary nerve sheath tumour of neuro-ectodermal origin.1 It usually arises from peripheral nerves and only rarely arises retroperitoneally. Forty-seven cases have been described in the English-language literature, of which all the relevant details have been documented in only 14 instances (Table I). Thus there is a paucity of specific information available regarding the retroperitoneal malignant schwannoma.

This case demonstrates many of the classic features of this type of tumour; the management of malignant schwannoma occurring retroperitoneally is discussed.

Case report

A 58-year-old white woman presented to the Johannesburg Hospital in January 1985 complaining of an enlarging lower abdominal mass, oedema and varicosities of the right lower limb, decreased appetite, significant weight loss, generalised malaise and decreasing effort tolerance and post-menopausal vaginal bleeding, all of 1 month's duration.

Clinically she was found to be cachectic. Oedema and varicosities of the right lower limb were noted. The abdomen was distended by a solid, ovoid, non-tender relatively mobile mass occupying the entire lower abdomen. It had a bosselated inferior aspect and a separate palpable mass at the upper margin. In addition there was a 1 cm hepatomegaly and a 1 cm splenomegaly. Vaginal examination revealed a large cystocele and a retroflexed fibroid uterus enlarged to the size of a 10-week pregnancy. A sulcus was noted between the anterior wall of the uterus and the inferior surface of the mass. On rectal examination the mass was felt impinging on the rectal wall but the rectal mucosa was free. No peripheral neuropathy was noted and there was no evidence of von Recklinghausen's disease.

Laboratory investigations showed normal full blood count and electrolyte, urea and creatinine levels; liver function tests were negative. The serum a-fetoprotein and carcino-embryonic antigen levels were also normal, but the serum lactic dehydrogenase level was raised to 217 U/l (normal < 200). The chest radiograph was normal. An excretory urogram showed the left kidney to be normal but demonstrated hydronephrosis of the right pelvicaliceal system with dilatation and lateral displacement of the right ureter (Fig. 1). A large mass was noted on the right side of the abdomen extending from the pelvis, where it indented the bladder fundus, to the renal area. Abdominal ultrasonography of the mass demonstrated a 16 x 15 x 11 cm solid cystic irregular mass. A barium enema was normal. Liver scanning with technetium-99m-tin colloid showed moderate hepatosplenoedymal with irregular filling defects in the antero-inferior aspect of the liver and patchy uptake suggestive of space-occupying lesions.

At laparotomy a large retroperitoneal tumour was found. The caecum and ascending colon were displaced to the left and anterior to the tumour. No abnormality of the liver was found and there was no ascites. Both ovaries were atrophic and the uterus was enlarged to the size of an 8 - 10-week cyesis as a result of an intramural fibroid. There was no evidence of any intra-abdominal tumour metastases.

The posterior retroperitoneum was opened vertically over the right paracolic area and the ascending colon displaced even further medially. The upper-third of the right ureter passed through the right upper lateral pole of the tumour causing compression and lateral displacement of the ureter. The tumour was dissected by freeing the right ureter by sharp dissection and dividing the nutrient vessels. The tumour was removed completely.

Fig. 1. Pre-operative excretory urogram showing hydronephrosis of the right pelvicaliceal system with dilatation and lateral displacement of the right ureter (left). Findings 6 weeks after surgery (right). Note resolution of the lumbar scoliosis, hydronephrosis of the right pelvicaliceal system and previous displacement of the ipsilateral ureter.

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TABLE I. MALIGNANT SCHWANNOMAS REPORTED SPECIFICALLY AS RETROPERITONEAL, ABDOMINAL PARAVERTEBRAL OR PERIRENAL TUMOURS

<table>
<thead>
<tr>
<th>Primary author</th>
<th>Yr</th>
<th>No.</th>
<th>Age(s) (yrs)</th>
<th>Sex</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retroperitoneal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Melicow²</td>
<td>1953</td>
<td>1</td>
<td>43</td>
<td>M</td>
<td>Biopsy</td>
<td>Died 4 d</td>
</tr>
<tr>
<td>Pack³</td>
<td>1954</td>
<td>1</td>
<td>5</td>
<td>F</td>
<td>S</td>
<td>NED 36 mo.</td>
</tr>
<tr>
<td>Carpenter⁴</td>
<td>1963</td>
<td>4</td>
<td>28 - 60</td>
<td>3F, 1M</td>
<td>S, 1 S + R</td>
<td>NED 7 mo.: 28 mo.: 96 mo.</td>
</tr>
<tr>
<td>White⁶</td>
<td>1971</td>
<td>2</td>
<td>35, 42</td>
<td>F, F</td>
<td>S + R</td>
<td>Died 4 mo.: 6 mo.</td>
</tr>
<tr>
<td>Moazam⁸</td>
<td>1983</td>
<td>1</td>
<td>14</td>
<td>M</td>
<td>S + C + R</td>
<td>Died 3 mo.</td>
</tr>
<tr>
<td>Present case</td>
<td>1985</td>
<td>1</td>
<td>58</td>
<td>F</td>
<td>S + C</td>
<td>NED 6 mo.</td>
</tr>
<tr>
<td>Paravertebral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Richards¹⁰</td>
<td>1979</td>
<td>1</td>
<td>?</td>
<td>M</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Perirenal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deming¹¹</td>
<td>1954</td>
<td>1</td>
<td>33</td>
<td>F</td>
<td>S</td>
<td>Died 18 mo.</td>
</tr>
<tr>
<td>Fein¹²</td>
<td>1965</td>
<td>1</td>
<td>51</td>
<td>F</td>
<td>S</td>
<td>Alive 24 mo.</td>
</tr>
<tr>
<td>Bair¹³</td>
<td>1978</td>
<td>1</td>
<td>56</td>
<td>M</td>
<td>S</td>
<td>Alive 7 mo.</td>
</tr>
<tr>
<td>Parfitt¹⁴</td>
<td>1982</td>
<td>1</td>
<td>63</td>
<td>M</td>
<td>S</td>
<td>Alive 7 mo.</td>
</tr>
</tbody>
</table>

? = not stated; F = female; M = male; S = surgery; R = irradiation; C = chemotherapy; NED = no evidence of disease.

Enlarged para-aortic nodes were selectively removed. A total abdominal hysterectomy, bilateral salpingo-oophorectomy and an appendectomy were performed.

The tumour weighed 3160 g and measured 30 x 22 x 7 cm. Macroscopically, it consisted of a lobulated mass of soft, pale tissue with numerous areas of necrosis. It appeared well circumscribed with the impression of a capsule. Histologically it showed a tumour of variable appearance. In many areas the cells were spindle-shaped with wavy nuclei and fibrillary cytoplasm. Numerous mitotic figures were present. There were occasional multinucleate giant cells. Other areas were more hypercellular, the cells having an oval appearance. There were extensive areas of tissue necrosis with some calcification. Other areas were sparsely cellular with a dense hyaline stroma. The tumour was not encapsulated and extended to the margins of excision. These features are compatible with a high-grade malignant schwannoma extending to the line of excision (Fig. 2). Immunoperoxidase stains for S100 protein were positive, confirming neural origin (Fig. 3).

Fig. 2. Fascicles of cells with buckled, spindled nuclei (H and E x 132).

Fig. 3. S100 protein, characterised by thin, black, wavy lines, in an immunoperoxidase reaction (x 528).

The uterus measured 15 x 7 x 4 cm with a large intramural fibroid 5 cm in diameter. Both fallopian tubes and ovaries were macroscopically normal as was the appendix and the 3 para-aortic nodes. Histological examination confirmed that there was no evidence of tumour in any of these organs.

The patient's postoperative course was uneventful. After recovery from surgery, chemotherapy was started. This consisted of dacarbazine 450 mg intravenously and adriamycin 60 mg intravenously weekly for 3 courses, and thereafter at 3-weekly intervals for 6 months.

Discussion

Malignant schwannomas, also known as neurofibrosarcomas, arise most frequently in the extremities, but they have been reported to occur in almost any anatomical location — retro-
peritoneal,\textsuperscript{23} paravertebral,\textsuperscript{9,10} perirenal,\textsuperscript{11-14} perineal,\textsuperscript{15} and in the stomach.\textsuperscript{16} Tumours originating in the retroperitoneum are rare, constituting only 0.01 - 0.2\% of all neoplasms.\textsuperscript{5,17} The vast majority are of soft tissue origin (fat or muscle), very few arising from nerve cells or fibrous tissue. It is notable that almost all retroperitoneal tumours are malignant,\textsuperscript{1} but malignant schwannomas represent less than 2\% of all primitive sarcomas arising in this region.\textsuperscript{18} It is uncertain, however, whether the malignant schwanna arises \textit{de novo} or from its benign counterpart.\textsuperscript{19}

An association between both the benign and malignant forms of the tumour and von Recklinghausen's disease is well documented.\textsuperscript{20} The tumour may develop in isolation as in this case. Clinically, the patients with associated von Recklinghausen's disease and those without form two distinct groups with regard to patient characteristics, location, histological findings and response to therapy. In a study of 165 cases of malignant schwannoma, Sordillo \textit{et al.}\textsuperscript{20} found 40\% to be associated with von Recklinghausen's disease. These patients were younger (median age 32 years compared with a median age of 48 years in the other group), had central rather than peripheral tumours, and had a lower 5-year survival rate of only 33\% compared with 47\%.

**Clinical presentation**

Goldman \textit{et al.}\textsuperscript{15} described the typical presentation of malignant schwannoma as a painless, slowly enlarging soft tissue mass occasionally associated with a peripheral neuropathy. Das Gupta and Brasfield\textsuperscript{4} reported that in their series of 232 patients 73\% of the tumours were painless.

Retroperitoneal malignant schwannomas present in a similar manner to other retroperitoneal malignant tumours, such as sarcomas. The features are poorly localised backache or abdominal pain and a palpable mass with or without fever, anaemia and/or weight loss.\textsuperscript{21} In those patients who present later, the symptoms may include ascites, lower extremity oedema and intestinal obstruction or ileus.\textsuperscript{14} Das Gupta and Brasfield\textsuperscript{4} utilised a three-stage classification for malignant schwannomas: stage I — intact primary tumour without evidence of local or distant metastasis; stage IIA — local recurrence at the site of earlier excision; stage IIB — extensive local recurrence; and stage III — distant metastases.

**Pathology**

Macroscopically there are no specific criteria by which a malignant schwanna can be identified definitively.\textsuperscript{5} It may, however, be possible to demonstrate the nerve of origin of the tumour from a larger nerve.\textsuperscript{22} Macroscopic demonstration of this neural origin may be important to differentiate the malignant schwanna from a fibrosarcoma,\textsuperscript{23} which it may resemble histologically.\textsuperscript{22,24,25} Unfortunately, however, in large retroperitoneal tumours the significance of nerve involvement can be particularly difficult to evaluate, especially where the nerve of origin is small.\textsuperscript{6} Clinically, in larger nerves a neural tumour can be suspected when a discrete mass can be moved in the transverse axis of the nerve but not the longitudinal axis.\textsuperscript{1}

A number of nonspecific macroscopic features have been recorded, viz. the grey-white colour, the well-circumscribed nature of this tumour which gives the appearance of a capsule (as in our patient), and a whorled or homogeneous cut surface, and focal areas of haemorrhage and necrosis. In addition, a large percentage of cases are associated with the physical stigmata of von Recklinghausen's disease.\textsuperscript{20}

Light microscopic features are also not absolutely diagnostic. There is a wide spectrum of features common to the malignant schwanna and other types of sarcoma, e.g. fibrosarcoma and leiomyosarcoma.\textsuperscript{22,24,25} Nonspecific features include: nuclear palisading (Antoni A tissue); loose fibrillar matrix (Antoni B tissue); and serpentine nuclear morphology.\textsuperscript{22,25} Furthermore, there may be well-defined mesenchymal heterotopic elements such as rhabdomyosarcoma, liposarcoma and osteogenic sarcoma, as well as areas of epithelial arrangement and gland formation.\textsuperscript{22,24,25}

Difficulty in assessing this tumour histologically is further complicated by the fact that schwannomas associated with von Recklinghausen's disease differ from those occurring in isolation.\textsuperscript{20} The former are characterised by a collagenous appearance with focal areas of nuclear palisading and rare areas of necrosis. Slender reticular and collagenous fibroblastic cells with long cytoplasmic processes predominate. They exhibit mild-to-moderate pleomorphism and occasional mitotic activity. By contrast these tumours in patients without stigmata of von Recklinghausen's disease are undifferentiated highly cellular neoplasms with 5 - 10 mitoses per high-power field. Palisading of the tumour cells is uncommon and stroma minimal.\textsuperscript{20} Positive immunoperoxidase staining for S100, a calcium-binding protein, serves to differentiate malignant schwannomas from other spindle-cell neoplasms such as leiomyosarcomas, spindle-cell carcinomas and malignant fibrous histiocytomas, all of which may cause diagnostic confusion on routine staining.\textsuperscript{26}

Electron microscopy has been suggested as the most definitive diagnostic modality currently available.\textsuperscript{14,22,24,25} It should, however, be used within the framework of a well-performed light microscopic study.\textsuperscript{27,23} Schwann cells have characteristic ultrastructural features, viz. profuse intertwining cell processes, sharply defined basal lamina formation, numerous microfilaments, granule and distinct cell junctions.\textsuperscript{22} Malignant Schwann cells are not as ultrastructurally differentiated.\textsuperscript{25}

The most consistent electron microscopic features of the malignant schwanna are: (i) slender overlapping cytoplasmic processes, which envelop other processes or cell bodies;\textsuperscript{24} (ii) conspicuous intracellular junctions,\textsuperscript{22,24,25} which are macular and zonula adherens and may also be seen in leiomyosarcomas but are notably absent in fibrosarcomas;\textsuperscript{24} and (iii) flocculent material assuming the form of a basal lamina in focal areas.\textsuperscript{25} Other electron microscopic features, viz. core-dense granules, intracytoplasmic filaments and long-spacing collagen,\textsuperscript{22,25} are of controversial diagnostic help.

The value of electron microscopy is determined by correct tissue sampling,\textsuperscript{25} hence the importance of associated histological studies. The major application for electron microscopy is for those tumours which are highly undifferentiated.\textsuperscript{25}

**Clinical course**

The tumours tend to be locally aggressive with frequent recurrence following surgical excision. Regional lymph node metastases are uncommon\textsuperscript{3} but may occur.\textsuperscript{8,7} There may also be intraneural and spinal subarachnoid dissemination.\textsuperscript{8,9} It has been suggested that metastases will not occur if the tumour continues to proliferate within the nerve sheath, while haematogenous spread may occur after penetration of the nerve sheath.\textsuperscript{1} Most frequently these metastases are to the lungs.\textsuperscript{18} Metastatic deposits have also been documented in liver, brain, bone, peritoneum, pleura, heart, adrenal gland, thyroid, spleen, kidney and intestine.\textsuperscript{20} The overall 5-year survival rate is 15\%; malignant schwannomas occurring near the central axis of the body are particularly lethal.\textsuperscript{7}

**Treatment modalities available**

At present therapy is radical surgical resection with adequate tumour margins.\textsuperscript{7,5} Solitary pulmonary metastases should also
be excised where technically feasible. Chemotherapy and radiotherapy may be added as adjuvant therapy. To date both these modalities are inconclusive. Some patients fail to respond while others show varying degrees of response, usually with subsequent relapse. Many chemotherapeutic combinations have been tried. These are summarised in Table II from which it can be seen that adriamycin is one of the most useful chemotherapeutic agents utilised in recent therapeutic regimens.

**Conclusion**

Retroperitoneal malignant schwannoma is an extremely rare tumour with few symptoms, making early diagnosis unlikely. Review of the literature reveals that treatment is primarily surgical with excision of adequate tumour margins. There is very little guidance in the literature as to the role of adjuvant therapy. In order to accumulate meaningful data to enable appropriate management of patients with this tumour we suggest that all cases are reported.

**REFERENCES**