Malignant Peripheral Nerve Sheath Tumor Presenting as a Massive Intra-abdominal Mass

Air Cmde PJ Vincent*, Lt Col S Rajagopalan†, Lt Col (Mrs) S Jetley‡, Maj (Mrs) A Sen**,
Wg Cdr P Singh (Retd)††, Surg Lt Cdr Rohit Sharma###

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Introduction

Malignant peripheral nerve sheath tumours (MPNST) have been designated by various names in the past including malignant schwannoma, malignant neurilemmoma, malignant neurofibroma, malignant neurofibrosarcoma, malignant mesenchymoma and neurogenic sarcoma. They usually present as large painful masses, are locally invasive, highly metastatic and obstruct the gut, ureters, blood vessels and so on. Criteria for diagnosis include demonstration of origin from a nerve, presence of Schwann cells, presence of neurofibromata, nuclear palisading on microscopy and immunohistochemical findings of S-100 protein. Resection and combination chemotherapy are the accepted modes of treatment [1]. There are many histological variants namely melanotic, epithelioid and a divergent variant with epithelial, glandular and mesenchymal differentiation. However, the cellular variant is considered benign [2].

Case Report

A 66 year old male patient presented with complaints of progressively increasing, painless, lower abdominal lump of more than three months duration. He gave no history of sudden increase or decrease in size of the swelling. There was a steady but unquantified weight loss but no jaundice, fever or urinary complaints. Bowels were normal and there was nothing to suggest any episode of bowel or urinary tract obstruction. Appetite was good. He did not report any chronic systemic illness.

On examination, the patient was elderly, weighing 60 kilos, and of average build and nourishment. Vital parameters were normal and there was neither icterus nor pallor. Mild pitting edema over the ankles and feet was recorded. A solitary, massive, firm, bosselated, non-tender intra-abdominal

mass extending between both iliac fossae laterally and from the umbilicus into the pelvis cephalo-caudally was palpable. The mass had restricted mobility in all the planes. No free fluid could be demonstrable. Liver, spleen and kidneys were not palpable. External genitalia was normal and systemic examination did not reveal any abnormality. Per-rectal examination was non-contributory.

On investigation, a complete haemogram and urinalysis were within normal limits. Biochemical investigations including urea, creatinine, sugar and liver function tests with all enzymes were within the normal range. A radiogram of the chest and ECG were normal. Barium enema and IVU did not reveal any lesion in the urinary tract or large bowel. FNAC of the mass was suggestive of a low-grade epithelial tumour probably a mesothelioma.

Ultrasound of the abdomen and pelvis showed multiple large lobulated heteroechoic masses in the abdomen in the umbilical, right and left iliac and hypogastric regions without any compression of the vessels or the urinary system. The masses appeared to be intra-abdominal rather than extra-peritoneal and the largest measured 12x9x12 cm. A 2.2 cm well-circumscribed target lesion was seen in the right lobe of the liver. No intra hepatic biliary radical (IHBR) dilatation was seen but a mild pelvicalyceal system (PCS) and ureteric dilatation were seen on the left side. Other organs were normal.

Contrast enhanced CT-scan showed multiple well-defined intra-abdominal hypo dense masses. Two of these masses were anterior to the psoas and seemed to occupy the entire lower abdomen and extended into the pelvis and insinuated anterior to rectum. Peritoneum was thickened at various sites with loss of intervening fat planes between the mass and anterior abdominal wall. There was hepatomegaly with poorly enhanced lesions scattered in the parenchyma. There was dilatation of ureters. Minimal ascites was seen. Other organs were normal. The impression given was multiple large intra-abdominal and pelvic masses with hepatic metastases and

*PMO, HQ(Southern Air Command), Trivandrum, †Associate Professor, ‡Ex-Associate Professor, Department of Surgery, Armed Forces Medical College, Pune-40, §Classified Specialist (Pathology), 151 Base Hospital, C/o 99 APO, **Medical Officer(Pathology), Command Hospital (Northern Command), C/o 56 APO, ###Graded Specialist(Surgery), INHS Kalyani, Vishakapatnam.

Fig. 1 : Photomicrograph of the tumour showing spindly as well as epithelioid areas (x 10)

Fig. 2 : Photomicrograph showing spindly area with nuclear palisading and moderate nuclear pleomorphism (x 40)

ascites probably of malignant origin.

The patient was taken up for exploratory laparotomy and debulking of the highly vascular tumour. Post-operative recovery was uneventful. He was thereafter put on palliative chemotherapy with alternating cycles of cyclophosphamide / doxorubicin and cisplatin / etoposide. Patient is doing well so far, pending further follow-up.

Histopathology revealed four masses with a combined weight of 4 kg. All masses showed surface bosselation, engorged vessels with grey-white areas of hemorrhage and necrosis, when cut. Microscopically, epithelial cells and spindle cells (Fig 1) with prominent nuclei and nucleoli with areas of nuclear palisading (Fig 2) were arranged in nodules surrounded by fibrous tissue (Fig 3). Mitotic figures were seen in 4/10 high power field. Areas of myxoid change, tumour cuffing of thin-walled blood vessels and necrosis were also noticed. Immunohistochemistry showed S-100 protein, focally positive (Fig 4) cytokeratin, melanin and negative epithelial membrane antigen (EMA). Impression was of a malignant peripheral nerve sheath tumour (epithelioid variant). Electron microscopic studies of the tumour cells showed cell membrane invagination combined with Schwannian differentiation (Fig 5).

Fig. 3 : Photomicrograph of epithelioid area showing plump cells with abundant cytoplasm separated by fibrous strands (x 40)

Discussion

MPNST make up 10% of all soft tissue tumours. Some workers record that up to 60% originate in pre-existing neurofibromatosis Type 1 lesions [3]. Our patient did not manifest any neurofibroma and the tumour seems to have originated *sui generis*. The presentation was atypical as there was no pain at any time, the mass was intra-abdominal and massive with no element of overt obstruction of any kind. Besides, there was no evidence of local invasion that is expected in such a massive tumour. Absence of these may cause diagnostic delay of upto 2 years [3]. Nerve sheath tumours can grow to giant sizes. Peabody et al report a schwannoma of 2.89 kg weight [4]. Our case was even larger, tipping the scales at four kilos.

One of the macroscopic criteria laid down for diagnosis is demonstration of nerve of origin at surgery. Dasgupta et al have observed that this is often not possible in view of the fact that they arise from small and insignificant nerves [5]. Nambisan et al could not demonstrate the nerve of origin in about 61% of their cases [6]. We tend to agree with them, as even we could not display any nerve of origin.

The treatment for MPNST has been combined modality that includes aggressive surgery with wide margin of clearance or mass debulking. Several cycles of adjuvant chemotherapy with cyclophosphamide / doxorubicin have been advocated [1]. However, Wanebo et al in their study of 28 cases advocate radiotherapy as adjuvant [7].

Immuno-histo-chemistry and electron microscopic studies [8] are gradually replacing histopathology as confirmatory diagnostic methods, as these tumours display a wide variety of histological patterns and hence no absolute standard is accepted. Studies by Matsunou et al have identified S-100 protein positivity and

Fig. 4: Immunohistochemical stain for S-100 showing focal positivity of tumour cells (x 40)

cytokeratin negativity as a supplementary tool for confirmation [9]. We are in full agreement with them.

In conclusion, our patient presenting with such a massive painless rapidly growing intra-abdominal tumour, in the absence of pre-existing benign neurofibromata, without evidence of local aggression, invasion or obstruction proved to be a diagnostic enigma. Imaging and FNAC not being very helpful, the final diagnosis rested only on histology and immuno-histo-chemistry of the specimen following surgery.

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Fig. 5 : Electron microscopic view of the tumour cells showing prominent cell membrane invaginations consistent with Schwannian differentiation (x 14,000)