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Retroperitoneal ganglioneuroma: a case report

Ganglioneuroma retroperitoneale: un caso clinico

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Summary

Retroperitoneal ganglioneuromas arise from the sympathetic ganglion cells and are usually considered as benign tumours. They develop as slow-growing abdominal masses and require a differential diagnosis supported by pathologic assessment. Because of their benign nature, adjuvant chemo-radiotherapy is not indicated in the treatment of ganglioneuromas for which carefully planned follow-up examinations are commonly suggested. Here, we report a case of a retroperitoneal ganglioneuroma treated with complete surgical removal. Eur. J. Oncol., 15 (1), 51-55, 2010

Key words: **ganglioneuroma, retroperitoneal, laparotomy, immunohistochemistry**

Riassunto

I ganglioneuromi retroperitoneali derivano dalle cellule gangliari simpatiche e solitamente vengono considerate neoplasie benigne. Presentano un lento sviluppo nel compartimento addominale e richiedono un'appropriata diagnosi differenziale coadiuvata dall'istopatologia. Data la loro bassa aggressività, non c'è indicazione a radio chemioterapia adiuvante, ma è consigliabile un stretto follow-up. Il caso clinico descritto si riferisce ad un ganglioneuroma trattato soltanto con resezione chirurgica completa. Eur. J. Oncol., 15 (1), 51-55, 2010

Parole chiave: **ganglioneuroma, retroperitoneale, laparotomia, immunoistochimica**

Abbreviations

CT: Computerized Tomography;
CEA: Carcinoembryonic Antigen;
TPA: Tissue Polypeptide Antigen.
AFP: Alpha-Fetoprotein;
CA19.9: Carbohydrate Antigen 19.9;
NSE: Neuron Specific Enolase;
CA 72.4: Carbohydrate Antigen 72-4.

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Background

Ganglioneuromas are considered as benign tumours characterized by poor proliferation rate and high differentiation mainly arising from sympathetic ganglion cells. They account for less than 1% of all soft-tissue neoplasms (1) and commonly appear in young population, particularly of female gender (2). Ganglioneuromas are frequently located in the posterior mediastinum or in retroperitoneal regions (3, 4) and may remain misdiagnosed in a similar fashion as for other retroperitoneal soft-tissue lesions.

Surgical removal is necessary for their definitive diagnosis and may concurrently represent an essential therapeutic choice (5). Because of the benign nature of ganglioneuromas, a careful follow-up is necessary for early monitoring their potential local relapse after resection.

Here, we report a case of ganglioneuroma extending from the retroperitoneum to pelvis, which remained undiagnosed before its excision.

Case Report

A 44-year old male patient was referred to our clinic complaining for two years continuous mild pain in abdominal regions. He reported no relevant medical history and no endocrinological symptoms like diarrhea, sweating and hypertension were present. No fever was claimed and the pulse rate was 80 beats per minute in the presence of normal blood pressure.

At physical examination, the patient appeared in well-being state. No skin rash neither lymphadenopaties were detected. Deep palpation of the abdomen revealed both normal size and consistency of liver and spleen, whereas a non-pulsatile mass was detected around the umbilical region. Bilateral hernia orifices and both testicles were apparently normal.

Routine laboratory tests showed hemoglobin of 14.1 g/dl, white blood cell count of 7670/mm^3 and blood sedimentation rate of 2 mm/h. Both urine and stool were normal. The serum total protein was 7.1 g/dl with albumin of 4.4 g/dl. The levels of urea nitrogen, creatinine, uric acid, total and conjugated bilirubin, alkaline phosphatase, aspartate aminotransferase and alanine aminotransferase were included within the normal range in a similar fashion as for tumour markers including CEA, CA 19.9, AFP, TPA, CA 72.4.

Abdominal ultrasonography revealed a defined hypoechoic solid mass of 10x4.5 cm, bilaterally at pre- and paraaortic/caval level, extending from the origin of renal arteries to the aorto-iliac bifurcation.

Abdomen and pelvis computerized tomography (CT) scanning, using intravenous contrast, confirmed the occurrence of a large homogeneously dense tissue arising in the abdominal retroperitoneum and spreading towards the pelvis with no bladder compression (fig. 1).

A first diagnosis of lymphoma originating from retroperitoneal nodes was suggested by the radiologist. However, a fine needle aspiration cytology examination of the lesion revealed only fibrotic tissue with a small number of Schwann cells. The patient was thus submitted to explorative surgical laparatomy. Intraoperative examination revealed 2 solid masses with diameter of 10x5 cm and 9x5.8 cm, respectively. The tumour emerged from the retroperitoneum and extended downwards to the pelvic peritoneum posterior to the bladder. On the cut section, both masses showed solid and grayish white surface. After excision, they were fixed in formalin for both histology and immunohistochemistry. These tests revealed that each tumour mass was composed by large mature multinucleated-ganglion cells with interlacing Schwann cell cords and collagen fibers (fig. 2). Immunohistochemistry using a panel of monoclonal antibodies revealed the expression of both S-100 protein and synaptophysin in tumour ganglion cells and in these sites the labelling index was less than 1%. Thus, the final histological diagnosis was ganglioneuromas of retroperitoneum.

Besides the surgical excision, no other treatments were adopted except the bimonthly follow-up. At present, ten months later the patient is asymptomatic with no evidence of relapse.

Discussion

Ganglioneuromas are included within the neuroblastoma group together with neuroblastomas and ganglioneuroblastomas, that originate from the

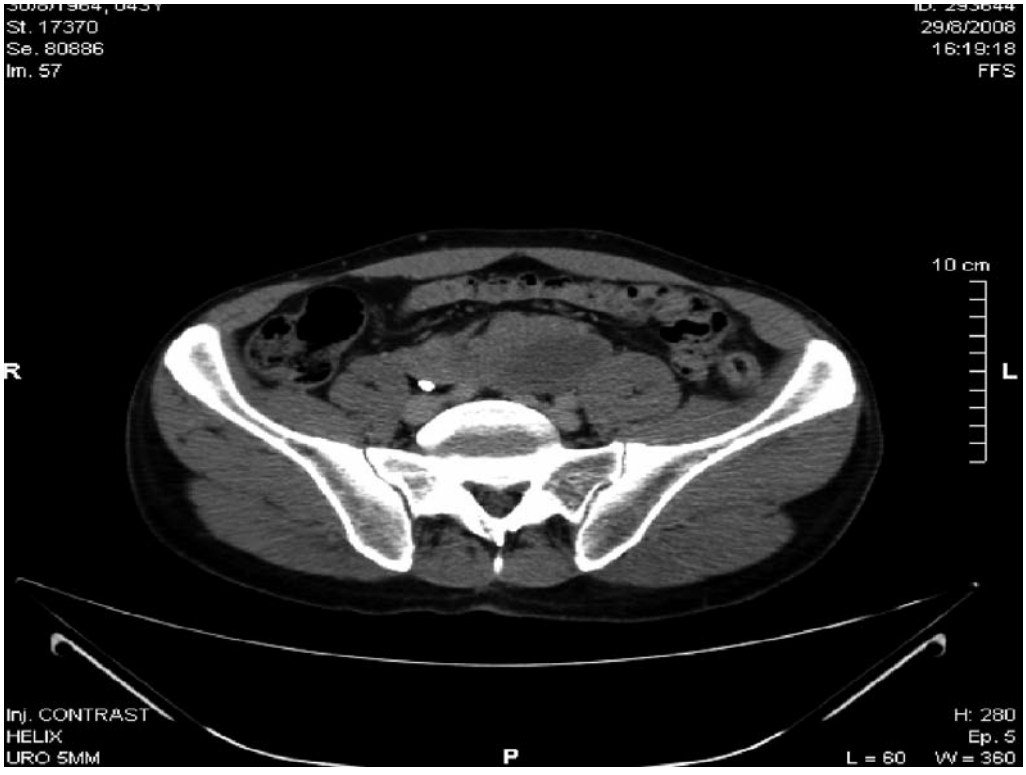

Fig. 1. CT scan shows a mass arising in the retroperitoneum (arrows)

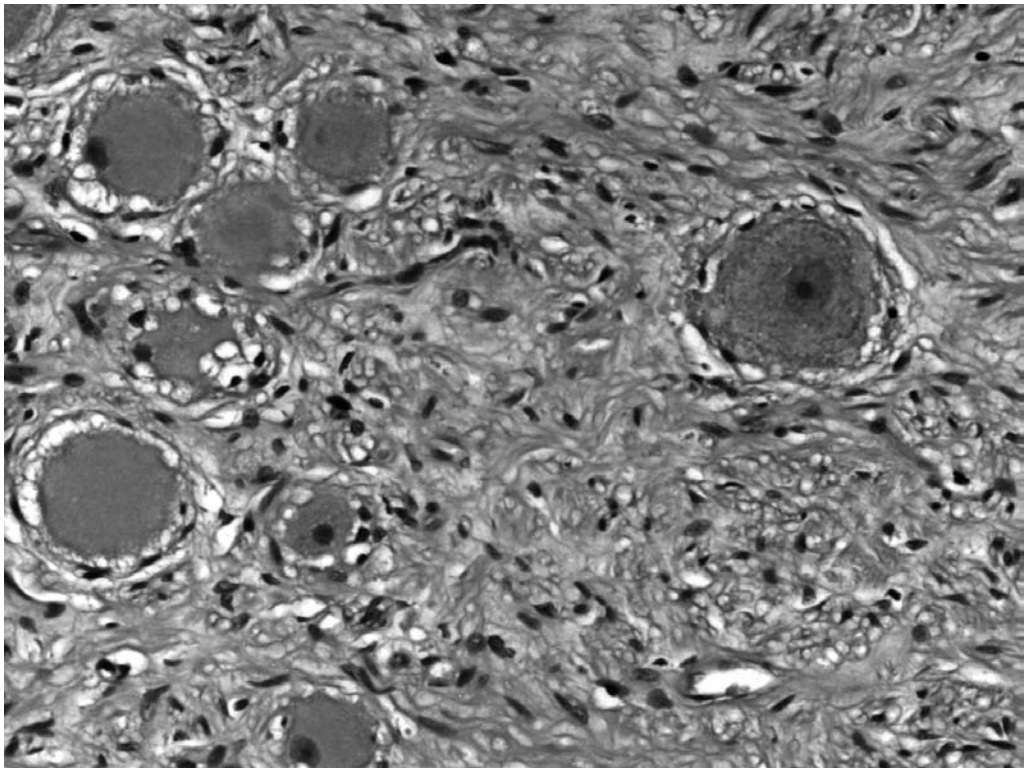

Fig. 2. Microscopic view of the tumour. The tumour was composed of ganglion cells (large size cells) with interlacing Schwann cell cords (small size cells) and collagen fibers

neural crest cells (2). Ganglioneuromas are well-differentiated tumours that represent the benign final evolution of the spectrum for the ganglion cell lineage, whereas ganglioneuroblastomas and neuroblastomas may account for the malignancies of this spectrum. They may also occur either spontaneously or during the treatment for neuroblastomas with chemotherapy or radiation therapy (6).

These rare tumours may appear at each age between 0 and 70 years although young females are

most commonly affected. Ganglioneuromas are prevalently localized within the posterior mediastinum followed by the retroperitoneum and usually recur at incidence as low as 1%.

Nonfunctioning retroperitoneal ganglioneuromas are usually asymptomatic until they grow to a large size and both epigastralgia and abdominal pain are claimed. On the contrary, functioning ganglioneuromas, releasing the vasoactive intestinal peptide (VIP), somatostatin or catecholamines, are generally accompanied with diarrhea, sweating and arterial hypertension (2, 7).

Recently, with the development of both ultrasonography and CT, reports of retroperitoneal ganglioneuromas have increased so far. The tumour often appears slightly hypoechoic on ultrasonography while homogeneous by CT. However, since the tumour fails to show typical sonographic aspects of radiologic features (2), these methods appear unreliable in the definitive diagnosis.

Because of the rarity of the retroperitoneal ganglioneuromas and the absence of typical radiologic features, their imaging can mimic a multitude of different conditions. In fact, the differential diagnosis of a retroperitoneal mass may include lymphoma, sarcoma, primary retroperitoneal germ cell tumour, in addition to metastatic cancers.

Lymphoma is the most frequent malignant tumour occuring in the retroperitoneum. Non-Hodgkin lymphomas recur at higher rate (93.7%) than the Hodgkin lymphoma (6.3%) and mostly affect middle-aged and elderly subjects. Patients with Burkitt's lymphoma (BL), or small-noncleaved-cell lymphoma, may show an intra-abdominal tumour and its short doubling time usually results in rapid progression (8). This peculiar pattern was not observed in our patient. Elevations of both lactate deydrogenase and uric acid that reflect high tumour burden and rapid cell turnover are commonly observed in patients with BL. The normal range of these tests in association with absence of fever, weight loss, pruritus and sweating, namely the prominent symptoms of BL, excluded this diagnosis in our patient.

Retroperitoneal sarcomas account for approximately 15% of all sarcomas (9, 10). The most common histological subtypes include liposarcoma and leiomyosarcoma. The majority of patients show abdominal masses whereas 50% of them claim moderate pain at the time of the presentation. These tumours often grow silently to a very large size before diagnosis. Patients typically refer chronic nonspecific symptoms related to the tumour compression rather than to the infiltration and those with sarcoma commonly develop metastases in both lungs and liver. Abdominal CT is particularly useful in the diagnosis. Sarcomas are frequently heterogenous and develop as irregular solid or semisolid, and liquefactive areas due to patchy necrosis. Thus, sarcomas may be highly suspected on the CT basis alone (11). Immunohistochemical detection of proteins typical of muscles tissue such as actin and desmin, or of blood vessels as factor VIII or of the epithelial tissue including membrane antigens and cytokeratins, may often help for a reliable tumour classification. However, radiological data of our case did not adequately support the sarcoma diagnosis.

Like metastatic retroperitoneal tumours, a number of clinical entities including renal, pancreatic cancers as well as advanced gastrointestinal carcinomas or germ cell tumours need to be considered. A detailed history and physical examination should include a testicular examination to exclude the testicular cancer with retroperitoneal metastasis. Moreover, laboratory tests should include the common serum markers for germ cell tumours like both beta-human chorionic gonadotropin (b-HCG), and alpha-fetoprotein (AFP).

When tumours appear to be derived from stomach, pancreas or duodenum, the gastrointestinal endoscopy with biopsy may be diagnostic. Likewise, colonendoscopy can be useful in diagnosing tumours arising from the colon. Absence of definite signs and the normal values of biochemical markers, however can exclude the occurrence of metastatic retroperitoneal tumours.

Preoperative CT- or ultrasonography- directed biopsy is invasive and rarely modifies the treatment choice in patients undergoing surgical exploration. However, specific circumstances in which a biopsy of primary retroperitoneal masses should be performed have to be considered (12). These include the clinical suspect of lymphoma or of germ cell tumour as well as potential retroperitoneal or intra-abdominal metastasis from another primary tumour.

Ganglioneuromas are generally well-circumscribed, solid, encapsulated masses of solid consistency with a solid grayish white at the cut surface. Microscopically, ganglioneuromas consist of bundles of longitudinally and transversely oriented Schwann cells with mature ganglion cells scattered throughout singly or in small nests. Immunohistochemically they are characterized by the detection of S-100 and other neuronal markers such as NSE and synaptophysin (13).

Although ganglioneuromas are benign tumours, adjuvant systemic chemotherapy or local radiotherapy have no value in the treatment. According to many authors, surgical excision represents the only choice for both diagnosis and treatment (5). Considering the potential growth of ganglioneuroma, in a patient with incomplete resection, despite a long-term disease-free period, a regular and prolonged follow-up is thus mandatory (14). If the progression of the tumour is somehow observed during follow-up, the re-biopsy or even laparotomy may be needed. However, the prognosis is generally good when completely resected.

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