Rare localization of malignant peritoneal mesothelioma

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Abstract
Peritoneal mesothelioma represents a rare disease, among its manifestations it can be encountered ascites and tumor abdominal masses and this condition, untreated can lead to death by bowel obstruction, perforation and cachexia. Due to the rarity of the disease, some patients are misdiagnosed and thus they cannot benefit from a radical form of treatment which leads to an increased survival. We hereby present the case of a 62 year-old male with previous surgery for a retroperitoneal tumor with relapse of the disease. The pathological examination and immunochemistry showed a diffuse peritoneal mesothelioma with poor differentiation. The patient was submitted to chemotherapy and 16 months after surgery on regular control imaging he presented a retroperitoneal recurrence. Unfortunately the patient refused the treatment; we believe that he could benefit from radical surgery associated with hyperthermic intraperitoneal chemotherapy. Preoperative diagnosis of diffuse peritoneal mesothelioma can be difficult due to the lowest predictability of the clinical and imaging studies.

Keywords: diffuse malignant peritoneal mesothelioma, immunohistochemistry, survival, intraperitoneal chemotherapy

Introduction
Diffuse mesothelioma represents a progressive disease of the pleura, peritoneum, vaginala testis and in rare cases of the pericardium, with an actual incidence of 1-2 cases per million [1]. Malignant mesothelioma represents 30% of all mesotheliomas [2] and it can be localized or diffuse. The disease has variable geographical incidence and in some cases it was described a familial aggregation of cases. There is a higher predominance in males (male/female ratio 1.9/1) [2], in 35% of cases a history of asbestos exposure can be encountered [3], but only a small percentage of patients exposed to asbestos develop the disease, probably due to a genetic susceptibility [4]. Other agents related to this condition are: exposure to thorotrust, talc, external radiation, Familiar Mediterranean Fever [5].

The peritoneal localization of the disease can manifest itself by unspecific abdominal complaints such as nausea, vomiting, weight loss, diffuse abdominal pain. On clinical examination can be encountered ascites or abdominal masses. Imaging studies such as echography and tomography can reveal ascites, thickening of peritoneum, eventual abdominal tumors with calcifications [6]. Moreover, the diagnosis is made during laparoscopy or laparotomy. Definitive diagnosis is made on pathological and
immunohistochemistry examination. There is no immunohistochemical marker with a high sensibility and specificity for malignant mesothelioma, often a combination of markers makes the diagnosis. For the epithelioid subtype the most frequent markers are: calcretinine, cytokeratin 5/6, podoplanin, WT-1 and trombomoduline [7]; for the sarcomatous subtype: cytokeratin 7, vimentine, cytokeratin 8/18, CAM 5.2, AE1/AE3 [8].

Due to the rarity of the disease the chemotherapy regiments are somehow similar to those used for pleural diffuse mesothelioma. In the absence of treatment the median survival is 6 months, with the aid of chemotherapy a median survival of 12 months can be expected [9]. Intraperitoneal hyperthermic chemotherapy associated with optimal cytoreduction has become the standard treatment for diffuse peritoneal mesothelioma with better results compared to systemic chemotherapy.

Case report

We hereby present the case of a 62 year-old male with previous radical surgery 2 years prior to admission for a right retroperitoneal tumour. The pathological examination showed a 7cm diameter solid tumour, on immunohistochemistry positive for CK AE1/AE3, synaptophysine and chromogranin. At that moment the diagnosis was extradigestive neuroendocrine tumor. The patient was not submitted to chemotherapy.

Seven months after the initial surgery, the patient was diagnosed with a recurrence of the disease; on imaging he presented a 10 cm in diameter tumor in the retroperitoneum. The tumor was considered unresectable on surgical exploration and multiple biopsies were performed. Pathological examination showed an undifferentiated carcinoma.

The patient was referred to our service for multidisciplinary treatment. On physical examination the patient presented an abdominal tumor on the topography of previous surgical scar, 10 cm in diameter. Laboratory test showed anemia (hemoglobin levels 9 mg/dl). Abdominal and thoracic tomography showed a large tumour with invasion of the abdominal wall, right colon, distal ileum, and the presence of two nodules on the greater omentum (Figure 1).

The conclusion of the multidisciplinary team meeting was that the patient could benefit from radical surgery due to the previous pathological examination (undifferentiated carcinoma).

![Fig. 1. Abdominal CT scan showing a large right retroperitoneal tumour](image-url)
On exploratory laparotomy, we found a large tumor on lower right quadrant without peritoneal carcinomatosis, except the two nodules described on tomography. It was performed en bloc resection of the tumor, a right colectomy, small bowel resection, part of the abdominal wall and omentectomy (Figure 2). The patient was admitted to intensive care unit and had an uneventful postoperative course. On immunohistochemistry the tumour was positive for calretinin (Figure 3), CK5 (Figure 4), CK7 (Figure 5) and negative for CK 20. Final diagnosis was diffuse malignant peritoneal mesothelioma, epithelioid type.

The patient was referred to chemotherapy and he received a standard treatment with included CDDP and Etoposide. On regular follow-up, 12 months after surgery, the patient was diagnosed with a retrogastric recurrence of the disease and he refused surgical exploration. The last follow-up was at 16 months after the last surgery.

Discussions

Due to the rarity of the disease, there are clinical and histopathological difficulties for the accurate diagnosis of this condition. Based on the histological subtype, the epithelioid subtype should be differentiated from the peritoneal or ovarian primitive carcinoma; the
sarcomatous subtype from the digestive or uterine sarcomas [10, 11].

The particularity of this case is the unusual initial localization of the tumor. The lack of data regarding the initial surgical approach (retroperitoneal, without exploration of peritoneal cavity) and findings makes a difficult accurate appreciation of the initial retroperitoneal localization of the disease. The tomography does not add a diagnostic benefit, due to the lowest sensibility for small peritoneal lesions. There were described in the literature inclusion ectopic peritoneal cells on retroperitoneum, but this condition occurs most often in female pelvis [12]. Another explanation can be that the patient presented a congenital mobile right colon, and the initial disease developed in the peritoneum in the right colic gutter. Moreover, in diffuse peritoneal mesothelioma there is the possibility of regional [13] or distant [14] lymph node metastasis, in our case the retroperitoneal tumour could have been an enlarged metastatic lymph node. This is unlikely, due to the dimension of the tumor and the description on histopathological examination. Nevertheless, one must keep in mind that there were described unusual localizations of the peritoneal mesothelioma [15]. On clinical and imaging evaluation of the patient, we did not have any suspicion that this condition could be a peritoneal mesothelioma.

Our patient underwent systemic chemotherapy; the best results in term of overall and disease free survival can be obtain with the combination Cisplatin-Pemetrexed [16]. Unfortunately the patient could not benefit from this combination, and it was administered a combination of Cisplatin and Etoposide.

For the last 35 years we witnessed a change of treatment options for peritoneal diseases. Large multicenter studies have showed that the best results are obtained in peritoneal mesothelioma by combining the optimal cytoreduction with hyperthermic intraperitoneal chemotherapy. The results of the largest study which included 405 patients showed a 3 and 5 years survival rates of 60 and 47%, the best prognostic factors being: the epithelioid subtype, the absence of lymph nodes metastasis, optimal cytoreduction and the hyperthermic intraperitoneal chemotherapy [17]. Morbidity and mortality rates for this highly demanding surgery are 39 and 2% [18], with a long learning curve [19] and with high costs [20]. It is difficult to evaluate the benefits of this intervention in our patient, without the appropriate diagnosis the patient was not referred to a specialized center.

We presented this case based on the rarity of the disease and the unusual localization of the tumor. Based on this patient previous surgical history we must keep in mind that any time we encounter a patient with an abdominal tumor in which the different imaging technique have discordant results, with normal serum markers and a negative exploration of the digestive tract, it can be a rare peritoneal disease. The real benefit of this high degree of clinical suspicion is a better multidisciplinary management which can provide the best results in term of survival.

Acknowledgement:

Dr. Huțanu Ionuț is a fellow of POSDRU grant no. 159/1.5/S/136893 with title: “Parteneriat strategic pentru creșterea calității cercetării științifice din universitățile medicale prin acordarea de burse doctorale și postdoctorale – DocMed.Net_2.0”.

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