MALIGNANT PERITONEAL MESOTHELIOMA
Case report and review of the literature

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SUMMARY

We describe a peritoneal mesothelioma. There are many aspecific symptoms. Professional exposure is found in only fifty percent of cases. The histological diagnosis is often difficult. The survival period is short because of the absence of curative treatment.

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INTRODUCTION

We report the case of a 59-year-old man who was admitted to the hospital with recurrent vesperal fever, anorexia, weight loss and abdominal distension. The complementary examination showed a malignant peritoneal mesothelioma. Histological diagnosis is difficult and needs complementary stains and further histochemical studies. Other exposure than professional exposure must be researched. The prognosis is poor despite of aggressive combination of therapies.

CASE REPORT

A 59-year-old man was admited to hospital with recurrent vesperal fever, profuse sweating, anorexia, weight loss, abdominal distension and signs of bowel obstruction. The symptoms had begun four days previously. Occupational exposure to asbestos was found twenty years ago, during seven years (building construction), and also during hobby work at home (during more than twenty years). The patient was not taking any medication.

On physical examination, the patient appeared emaciated. He was afebrile. Pulmonary auscultation was negative. We found one left cervical lymphadenopathy. The abdomen was distended and there was mild diffuse tenderness. Bowel sounds were absent.

Biological results in the emergency room showed: inflammatory blood chemical findings, thrombocytosis, negative bacteriology, negative tumoral markers. Plain abdominal radiographs suggested small bowel obstruction. Further tests were undertaken. The urogenital check-up was negative. Pulmonary examinations were as follows: bronchoalveolar lavage revealed the presence of asbestos fibers. Multiple sputum cultures were negative. Chest X-rays were normal. The complementary digestive examination was contributive. The abdominal computed tomography suggested a thickening of both epiploon and mesenterium, with a pseudotumoral appearance. The colonoscopy suggested diverticulitis. At laparoscopy, we found diffuse peritonitis in association with spreading of nodular lesions; biopsies were undertaken (Fig.1).

Histological examination included two stages. First, hematoxylin stain (original magnification x40) showed epithelial structure with nuclear abnormalities, suggesting the diagnosis of adenocarcinoma or carcinomatous lymphangitis (Fig.2). Subsequently, complementary stains and further immunohistochemical studies (Periodic Acid-Schiff coloration, Blue Alcian

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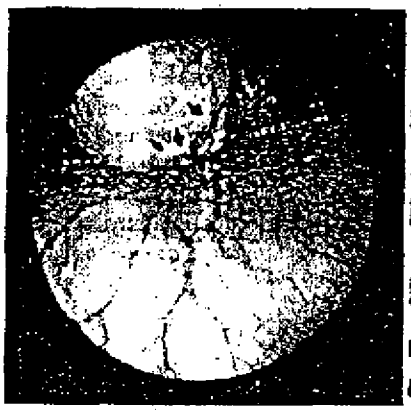

Fig.1. Laparoscopy: visualisation of nodular lesions on the serous side of the large bowel.

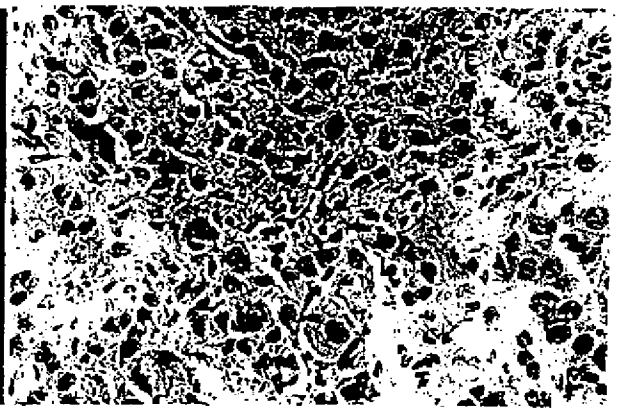

Fig.2. Hematoxylin-eosin stain (magnification X 40): characteristic epithelial structure.

coloration, Monoclonal anti-Carcino-Embryonic-Antigen (CEA) Antibody, anti-Keratin 8 and 18 antibodies) suggested epithelial malignant tumour compatible with mesothelioma.

In spite of rapid chemotherapies (cyclophosphamid-adriamycin twice), death occurred four months later.

DISCUSSION

Malignant mesothelioma is a rare disease with an incidence in the United States of 2.2 per million per year (1,4,5). Primary peritoneal mesothelioma accounts for 10% to 20% of all mesotheliomas (1-5). Mesotheliomas arise from pluripotential progenitor cells and may occur in the pleura, pericardium, peritoneum and tunica vaginalis testis.

Asbestos exposure seems to constitute the primary cause of both pleural and peritoneal mesothelioma (PM) in humans. Risk relates to the duration and intensity of exposure (12). Previous asbestos exposure is found in 0% (1) to 83% of cases. In some reports, the link between asbestos and peritoneal mesothelioma is not clear (4) especially for pediatric population, suggesting other etiologic factors than occupational exposure, such as environmental and familial exposure (5). In 1993, Dawson stated that the pathology of malignant mesothelioma appears to be similar in men and women, and in cases associated and unassociated with asbestos (8). Other associated exposure or disease include talc, mica, thorotrast, X-ray, recurrent peritonitis due to familial Mediterranean fever, and diffuse lymphocytic lymphoma (2).

The mean age varies from 49 to 59 years. The median interval between first exposure to asbestos and diagnosis varies from 27 to 52 years. The mean duration of exposure also varies from 11 to 28 years (1-6).

Symptoms are aspecific: abdominal pain, dysphagia, weight loss, malaise, anorexia, fever, weakness, signs of bowel (sub)obstruction, and abdominal enlargement. More specifically, ascites is found in 33% to 90% of cases (3,4). An abdominal mass may be palpated in 13% to 29% of cases (1,4).

Laboratory findings are not helpful in making the diagnosis. Some reports describe polyclonal hyperimmunoglobulinemia (5), thrombocytosis (by persistent secretion of interleukine-6) (2), ectopic hormonal production (insuline-like substance, growth hormone, antidiuretic hormone)(1,5). Radiographically, CT-scan images are not specific. PM may have multiple manifestations on CT-scan: abdominal mass, scattered

intraabdominal nodules, thickening of mesenterium. The CT-scan's value lies in its ability to direct sites of biopsy and to measure response to therapy (9). The diagnosis of mesothelioma is usually made at the time of laparoscopy or laparotomy. Cytological examination of ascitic fluid fails to give diagnosis; nevertheless, van Gelder reports positive cytologies of ascitic fluid in 26% of cases (3). The histological examination permits the differentiation of three lesions, by order of frequency: epithelial (37 to 75%), mixed (19 to 42%), fibrous (2,5 to 21%) (1,4,6,9,12). Vogelzang describes in his study a classically biphasic histology of mesothelioma, with both epithelial and sarcomatous areas present (7). Other more benign forms of PM exist, such as well differentiated papillary mesothelioma of epithelial subtype and cystic mesothelioma (CM).

CM of the peritoneum is a well recognized but rare tumor, the mesothelial origin of which has been suggested by recent ultrastructural studies (16). CM seems to occupy a borderline position between benign adenomatoid tumor and malignant tubulopapillary mesothelioma (16). It occurs mostly in the female population (89%), and mean age is 38 years. The most frequent complaint is an abdominal mass (16,17). CT-scan more accurately demonstrates its location and extent. Diagnosis is made by laparotomy; this tumor has a clear predilection for the peritoneum and the omentum of the pelvic viscera. In all cases, surgical resection is uncomplicated. No fatal cases have been reported. CM is not chemo- or radiosensitive. Recurrence occurs in 26% of cases (16,17). Differential diagnosis must be done with lymphangioma, ovarian cystadenoma or cystadenocarcinoma, teratoma, cystic smooth-muscle tumor and endometriosis.

Malignant mesothelioma is difficult to diagnose. Classic Hematoxylin-eosin stain fails to give diagnosis. Alcian blue staining for hyaluronic acid secreted by mesothelial cells is a good alternative. Exclusion of intracellular mucin with a Periodic Acid-Schiff stain usually rules out carcinoma (2). Immunohistochemical studies currently have a role in the routine diagnosis of malignant mesothelioma (MM). Numerous monoclonal and polyclonal antibodies reactive with mucosubstances, lectins, intermediate filaments (keratins), cytoplasmic or membranous oligosaccharide, are now available and may be applied to routinely fixed and paraffin-embedded tissues (11). Sheibani et al. describe in his report a series of antibodies, permitting the differential diagnosis between MM and adenocarcinoma (10): Leu-M1 Antigen, Monoclonal Antibody B72-3, Human Milk Fat Globules (HMFG-2), Carcinoembryonic Antigen, Anti-Keratins, Vimentin, Monoclonal Antibody Ber-EP4, Monoclonal Antibody 44-3A6, Lectins, Antimesothelioma Monoclonal Antibodies. On the other side, electron microscopy makes the diagnosis easier by revealing the characteristic ultrastructural elements: basement membrane, desmosomes, microvilli (4).

In a large autopsies' series, it is determined that local invasion (gastrointestinal tract, abdominal wall, liver, pancreas, diaphragm and retroperitoneum) and metastases (lymph nodes, liver, lung, pleura, pericardium, heart, adrenal glands) are common (1-3,5,6). In two studies (12,13) we found a relationship between histological classification and lung asbestos fiber content; PM seems to be associated with higer doses (12). In the second study, the authors conclude that a dose-response relation appears to exist, but that threshold must be determined by the life span of the person exposed (13). The mean survival fluctuates around 12 months in most of series, because of the absence of curative therapy. The review of Fraire et al. who analyse mesothelioma in childhood suggest a negative prognosis with a survival rate of 30% after one year (14).

For the treatment, some studies marginally describe an improvement of the survival with aggressive combination of therapies:

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- combinated chemotherapies like Doxorubicin-Cisplatin or Mitomycin-Cisplatin;

- the association surgery-intracavitary ^{32}P-Adriamycin(18).

In conclusion, this case is interesting because of its rarity, the acute presentation, the short professional period of exposure, but also the short period of survival despite of epithelial form with better prognosis and rapid chemotherapies. Exposure to asbestos must be researched; there may be professional, environmental and familial (hobby activity, family and workers) exposures. Nevertheless, other causes of MM must be kept in mind (mica, talc, thorotrast, X-ray, recurrent peritonitis due to familial Mediterranean fever,...). Diagnosis is difficult because of the absence of specificity of symptoms. Electron microscopy, immunohistochemical studies and analysis of lung asbestos fiber content are helpful in the chain of diagnosis. The prognosis is poor despite of aggressive combination of therapies and therefore innovative new approaches are needed.

RESUME

Nous décrivons un mésothéliome péritonéal. Les symptômes en sont divers et aspécifiques. Une exposition professionnelle n'est retrouvée que dans 50% des cas. Le diagnostic histologique est souvent difficile. La survie moyenne est courte, en l'absence de thérapeutique curative.

SAMENVATTING

We beschrijven een peritoneaal mesothelioma. De symptomen zijn verschillend en aspecifiek. Professionele expositie is slechts in 50% van de gevallen teruggevonden. De histologische diagnose is dikwijls moeilijk. De gemiddelde overleving is kort aangezien er geen curatieve behandeling is.

REFERENCES

1. Brenner J, Sordillo PP, Magill GB et al. Malignant peritoneal mesothelioma. *Am J Gastroenterol.* 1981; 75: 311-3.
2. Chahinian AP, Pajak TF, Holland JF et al. Diffuse malignant mesothelioma. *Ann Intern Med.* 1982; 96: 746-55.
3. van Gelder T, Hoogsteden HC, Versnel MA et al. Malignant peritoneal mesothelioma: a series of 19 cases. *Digestion.* 1989; 43: 222-7.
4. Plaus WJ. Peritoneal mesothelioma. *Arch Surg.* 1988; 123: 763-6.
5. Asensio JA, Goldblatt P, Thomford NR. Primary malignant peritoneal mesothelioma. *Arch Surg.* 1990; 125: 1477-81.
6. Kannerstein M, Churg J. Peritoneal mesothelioma. *Hum Path.* 1977; 8: 83-94.
7. Vogelzang NJ. Malignant mesothelioma: diagnosis and management strategies for 1992. *Semin Oncol.* 1992; 19 (Suppl): 64-71.
8. Dawson A, Gibbs AR, Pooley FD et al. Malignant mesothelioma in women. *Thorax.* 1993; 48: 269-74.
9. Smith TR. Malignant peritoneal mesothelioma: marked variability of CT findings. *Abdom Imag.* 1994; 19: 27-9.
10. Sheibani K, Esteban JM, Bailey A et al. Immunopathologic and molecular studies as an aid to the diagnosis of malignant mesothelioma. *Hum Pathol.* 1992; 23: 107-16.
11. Donna A, Betta DG, Bellingeri D et al. New marker for mesothelioma: an immunoperoxidase study. *J Clin Pathol.* 1986; 39: 961-8.
12. Leigh J, Rogers AJ, Ferguson DA et al. Lung asbestos fiber content and mesothelioma cell type, site and survival. *Cancer.* 1991; 68: 135-41.
13. Craighead JE, Mossman BT. The pathogenesis of asbestos-associated diseases. *N Engl J Med.* 1982; 306: 1446-54.
14. Fraire AE, Cooper S, Greenberg SD et al. Mesothelioma of childhood. *Cancer.* 1988; 62: 838-47.
15. Ackerman LV. Mesothelial and related neoplasms in children and adolescents: a clinicopathologic and immunohistochemical analysis of eight cases. *Pediatr Pathol.* 1992; 12: 333-47.
16. Katsube Y, Mukai K, Silverberg SG. Cystic mesothelioma of the peritoneum. *Cancer.* 1982; 50: 1615-22.

17. O'Neil JD, Ros PR, Storm BL et al. Cystic mesothelioma of the peritoneum. *Radiology*. 1989; 170: 333-7.

18. Ledreman GS, Recht A, Herman T et al. Long-term survival in peritoneal mesothelioma. The role of radiotherapy and combined modality treatment. *Cancer*. 1987; 59: 1882-86.