Lung cancer is the most common cause of cancer-related death in industrialized countries. Annually in the world, 1.1 million new cases are diagnosed (1) and almost 50% of these patients already have, at the time of diagnosis, metastases localized to the brain, liver, adrenal glands, bones, and lymph nodes. As autopsy cases reveal, gastrointestinal metastasis from lung cancer occurs with frequencies between 2 and 14% (2-6); this figure reduces significantly when considering only the symptomatic intestinal sites (2,7). In 1986, McNeil (6), considering only the metastases in the small intestine, noted that until then, only 9 symptomatic cases were reported in international literature, and Berger (8) in 1999 reported no more than 50 cases. At the moment, in literature only individual cases of repetitions in the intestine of a patient with lung cancer are reported (1).

The following is a case of a patient with a symptomatic repetition of a lung cancer in the small intestine, which, even less frequently, is the first clinical manifestation of the primary tumor.

Case report

R.S., male, 73 years old. The patient reported, starting about 2 months prior, the onset of intense pain in the mesogastric area. He was then hospitalized in our department due to the onset of intestinal obstruction with diffuse abdominal pain. The physical examination revealed hard swelling on the right side of abdomen. Abdomen was painful to the touch, mobile, and non-pulsating. Immediately after admission, the patient underwent a CT scan of the abdomen and chest with contrast medium showing:

1. in the abdomen:
   - marked concentric thickening and enhancement of the wall with stenosis of the penultimate ileal loop; a branch of the superior mesenteric artery and superior mesenteric vein both afferent and efferent to the lesion appear hypertrophic (Fig. 1);  
   - the presence on the right adrenal gland of a rounded swelling, with regular margins, with a maximum diameter of about 28 mm, with thin wall enhancement (possibly an adenoma?);
   - modest quantity of free abdominal fluid;
2. in the chest:
   - in the anterior mediastinum, on the left side, the presence

SUMMARY: Primary neuroendocrine lung tumor presenting with acute ileal obstruction. Case report.

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The authors describe a clinical case of a patient with neuroendocrine carcinoma of the lung diagnosed after the onset of an intestinal obstruction from an ileal metastasis. A review of literature reveals that the incidence of symptomatic gastro-intestinal metastases from lung cancer has been estimated to be about 2-3% and is exceedingly rare that the intestinal symptoms may be the initial presentation of cancer of the lung.

The authors emphasize the difficulty of preoperative diagnosis of gastro-intestinal metastases which is made, almost always, too late because of the lack of specific symptoms. In our case, on account of the computed tomography, we leaned towards the diagnosis of lymphoma because of the double mediastinal and abdominal localization. Furthermore, this diagnosis was supported by the fact that the pulmonary lesion did not have clear radiological features of a lung cancer.

The prognosis is poor because once intestinal metastases occur, other metastatic sites, which would make surgery only a palliative measure, are already present. The review of the literature shows that the average survival rate of these patients is 136 days. In our case the patient survived 277 days.

KEY WORDS: Intestinal obstruction - Lung cancer - Metastases - Survival.
Primary neuroendocrine lung tumor presenting with acute ileal obstruction. Case report

A mass (maximum axial diameters of about 97x78 mm) of parenchymal density, with central hypodense areas due to probable colliquative necrotic phenomena; the above mass leans against the cardiac structures anteriorly, without being infiltrative:

• in the posterior basal segment of the right-lower lobe, against the pleura of the vertebral canal, a circular pseudo-cystic area is noticeable (41x27 mm) with regular margins, dishomogeneous, potentially related to the fibrous scar area, although other diagnosis are conceivable (Fig. 2).

Radiological diagnosis: the findings described could be compatible with a lymphomatous process in the ileal and mediastinal areas.

Spirometry:
- FEV1: 2.12; FVC: 2.23; FEV1%: 95; MV V: 95.

Diagnosis: mild restriction.

Tumor markers:
- CEA: 34.4 (nv <3.4);
- CA 19.9: 58.7 (nv <34);
- CA 15.3: 57.6 (nv <25);
- CA 125: 50.62 (nv <35).

Surgery, performed urgently 10 hours after admission, started with a median laparotomy which showed the presence of a bulky lesion that encompassed three ileal loops. The ileum was resected from the upper and lower extremities of the mass and subsequently a lateral-side mechanical anastomosis was performed.

Histological examination (Fig. 3) of the removed ileal intestine allowed for a diagnosis of a “metastatic neuroendocrine carcinoma probably of pulmonary origin (TTF-1, synaptophysin and chromogranin A positive, CDX-2 negative)”.

At 20 days after surgery the patient underwent:
- a CT-guided needle biopsy of the pulmonary lesion which confirmed the presence of a lung neuroendocrine carcinoma;
- a CT scan of the brain which showed the presence of multiple cerebral metastases.

The patient died 9 months (277 days) after surgery without undergoing further treatment.

Discussion

The incidence of gastro-intestinal metastases from lung cancer has been estimated, in autopsy studies, to be about 10%. This percentage is reduced to 2-3% when looking only at metastases which cause bowel symptoms (2,4,7-11). More specifically, McNeil (6) reported that 431 autopsies of patients who died from lung cancer showed intestinal metastases in 10.7% of cases, only 1.4% of which were symptomatic; likewise, Yoshimoto (12), in a recent series of 470 autopsies, reports respective percentages of 11.9% and 2.6%. With regards to our case, it also seems appropriate to emphasize that it is “exceedingly rare” (10) that the intestinal symptoms may be the initial presentation of cancer of the lung. McNeill (6), Berger (8), Gomez-Patino (9), and Rossi (10) show, in their series of lung carcinomas, frequencies of 0.02%, 0.07%, 0.2%, 0.5% while more numerous authors do not record any case of lung cancer with this type of presentation (2,4,7,13,14).

The small intestine is the site of a greater number of metastases of blood or lymph origin (1,7) of a carcinoma of the lung even though it is still debatable whether the jejunum or ileum, as in our case, is more involved (2,4,8). The histological type of lung cancer that most frequently causes metastases of the intestine is not known because most authors do not record specific histological prevalence in their series or reviews of literature (3,7,8,10,11,13). Others, however, sometimes report a prevalence of the squamous cell carcinoma (4,6) and at other times adenocarcinoma (2) or large cell carcinoma (12). No author cites the neuroendocrine carcinoma of the lung as the principle type of an intestinal metastasis.

The diagnosis of intestinal metastasis from lung cancer often comes late; this results in the need for the urgent intervention which this type of localization almost always requires as it usually appears either with a hemorrhage caused by ulcerative action of the tumor, with a perforation caused by a necrotic action, or even more...
frequently (11,15) with an intestinal obstruction caused by proliferation which is in turn brought on by the metastases. Also, if the bleeding is often the presenting symptom for locations in the higher and lower gastro-intestinal tract, the site in the small intestine is often a cause of perforation or occlusion (2,4,10,13) as occurred in the case referred to in this article. The reasons for a late diagnosis stem from the fact that a bowel metastasis from lung cancer is rarely suspected despite a substantial rate, as the previously-mentioned autopsy findings have shown; moreover, the symptoms are not specific nor are the radiologic methods such as small bowel enema or CT very perceptive especially for small tumors (3).

In our case, in light of the CT, we leaned towards a diagnosis of lymphoma because of the double mediastinal and abdominal localization. Another factor which led to our decision was that lymphoma is frequently the cause of a primary tumor of the small intestine (10), and it is presently impossible to be able to differentiate preoperatively from another metastatic tumor (3). Furthermore, this erroneous diagnosis on our part was supported by the fact that the pulmonary lesion diagnosed on the CT, even though suspected, was small (compared to a mediastinal or abdominal mass) and did not have clear radiological features which would have led us towards a diagnosis of primary lung cancer. In addition, the urgent nature of the case did not allow for more extensive diagnostic investigations such as Positron Emission Tomography (PET), video capsule endoscopy or double-balloon endoscopy (2,4,7), methods whose use is controversial even to this day (5,12) and that in any case constitute diagnostic investigations of a secondary level. In our case, the histological examination is what changed our diagnosis in that it showed a neoplastic small cell with a polygonal shape, a relatively low nuclear-cytoplasmic ratio (N/C), coarse nuclear chromatin, and frequent nucleoli arranged in organoid nests, trabeculae, and rosettes, often with palisading of the nuclei at the periphery of the nests; high mitotic rate and frequent necrosis was seen.

The immunohistochemical profile showed strong positivity for synaptophysin, chromogranin A and TTF-1 and negativity for CDX2. TTF-1 is a transcription factor selectively expressed in thyroid and pulmonary epithelial cells which may assist in distinguishing lung carcinoma from some nonpulmonary carcinoma, especially when it is used in conjunction with CDX-2.

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These results, in conjunction with morphological features which excluded any involvement on the part of the thyroid, suggested the diagnosis of poorly differentiated neuroendocrine carcinoma probably from primary lung cancer.

In the history of a lung tumor, a metastasis of the small intestine indicates a “dire” prognosis (13) because it tends to occur at an advanced stage of lung disease when other metastatic sites are often signs of a systemic spread (3,5).

In his autopsy cases, McNeil (6) makes mention of an average of 4.8 extra-pulmonary metastatic sites present at the time of diagnosis of a repetition of the gastrointestinal tract while many authors report that most of their patients had at least one other metastatic site at the same time (4,7,8,14). In our case, the lung cancer, in addition to the ileal repetition, had led to extensive mediastinal lymph node involvement, brain metastases, and possibly adrenal ones as well.

If we analyze 31 patients, collected from the literature, treated for a gastrointestinal metastases from lung cancer (2,4,7,13), we can record a median survival rate of 136 days with a peak, reported by Kim (7), of 33 months. Such poor survival rates, added to a perioperative mortality which is often high (11), will inevitably lead doctors to have to choose between opposing solutions such as aggressive treatment or abstention, or even to reflect on the extent of surgical resection or on use of complementary systemic post-operative therapies (13,16). From this point of view, the selection of patients suffering from gastrointestinal metastases seems to be essential, and in this regard at least two elements may be used, one being the presence or absence of other metastatic ex-
tra-pulmonary sites, and the other, the way in which the intestinal relapse manifests itself because of the obvious fact that a perforation, which leads to peritonitis and shock, for example, will impact on the patient in a more disruptive way (10,13).

When we consider ever-increasingly specific and effective therapies for a cancer of the lung, it becomes likely that the survival rate of patients with such disease will improve over the years, and in light of this fact it is also clear that the number of patients with extrapulmonary metastases, including cases which concern the gastrointestinal tract, will increase as well. The goal should therefore be to improve diagnostic methods so as to allow for a more accurate diagnosis of this type of relapse, which must be identified before becoming symptomatic. This must be done by way of earlier diagnoses which can lead to surgical treatment and thereby improve survival rates in ways still unthinkable today.

It need not be mentioned that when dealing with so rare a disease it is impossible to simply follow guidelines; any decision and approach regarding treatment must be examined according to the individual case (13) and delegated to the experience and judgement of each individual team.

Acknowledgements and disclosures

The Authors declare that they have no conflict of interest.

References