Bratisl Lek Listy 2008; 109 (12)
576 – 579

CASE REPORT

An unusual presentation of testicular cancer

Vertakova Krakovska B[1,2], Usakova V[1], Hvizdakova A[3], Spanik S[1], Svec J[4]

Department of Clinical Oncology, St. Elizabeth Cancer Institute, Bratislava, Slovakia.
bibianakrakovska@gmail.com

Abstract: We report two rare cases of patients presenting with unusual symptoms, which led to the diagnosis of a germ cell tumor. Metastatic germ cell tumor of testis involving the gastrointestinal tract and causing the occult gastrointestinal bleeding is described in the first case. The second patient is reported to have limbic encephalitis with positive serum for Ma2 antibodies (antibodies against neuronal proteins) and parallel malignant germ cell tumor diagnosis *(Fig. 4, Scheme 2, Ref. 12)*. Full Text (Free, PDF) www.bmj.sk.
Key words: germ cell tumors, testicular cancer, gastrointestinal metastases, paraneoplastic limbic encephalitis.

Seminomatous or nonseminomatous (NSGCT) germ cell tumors are the most common malignancy in men aged 15–35 years, 5 % of these tumors are of the extragonadal origin (1). Seminomas account for one half of all testicular germ cell tumors. Embryonal carcinomas, teratomas, choriocarciomas, and yolk-sac carcinomas belong to NSGCT.

Regional metastases appear first in retroperitoneal lymph nodes below the renal vessels. Right-sided testicular tumors spread to the right paracaval and retrocaval nodes. Only rarely (aproximately 5 %) are metastases found in gastrointestinal tract (2). Invasion and compression of duodenum by lymph node metastases is a rare complication and is more likely related to right-sided testicular tumors. It often presents with an occult gastrointestinal bleeding or bowel obstruction. Left-sided tumors also spread to lymph nodes around the great vessels (3).

Paraneoplastic neurological syndromes, e.g. paraneplastic limbic encephalitis (PLE) associated with carcinoma are rare. Combination of paraneoplastic limbic encephalitis and the anti Ma2 antibody detection is associated with testicular cancer even in the subclinical stage (4). Other common sites of metastases are lung, liver and brain.

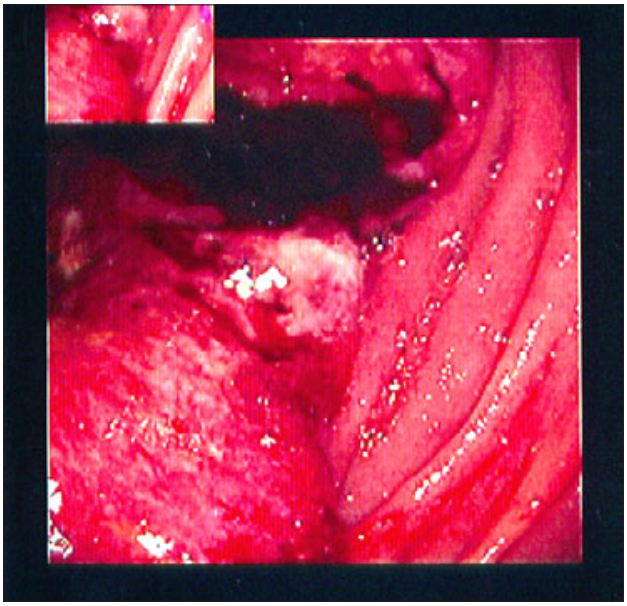


Fig. 1. Fragile solid tumor of proximal jejunum.

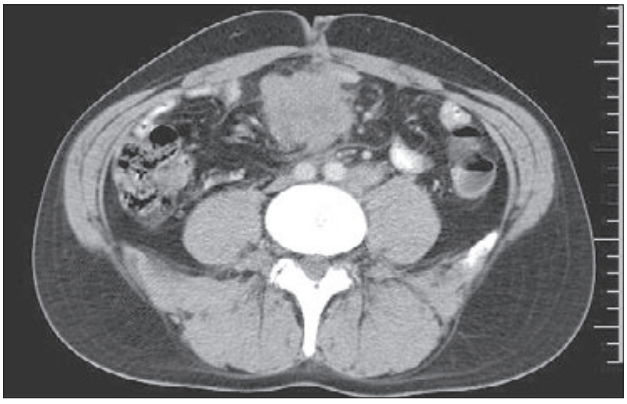


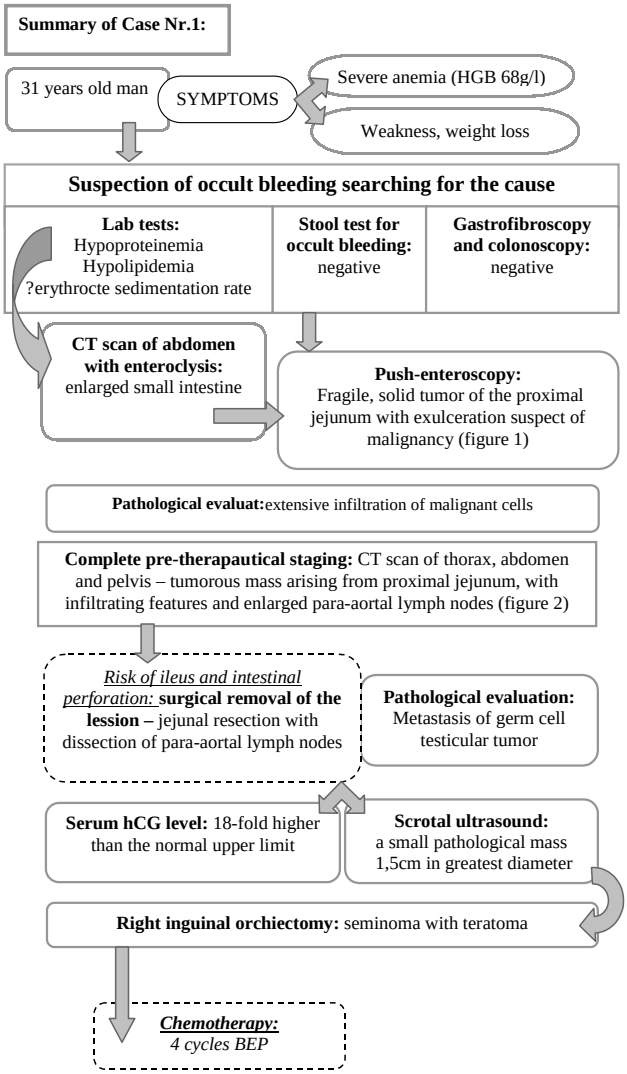
Fig. 2. Abdomen CT scan – tumor arising from proximal jejunum.

Case report 1

A 31-year old man suffering from weight loss, weakness and worsening in physical performance presented with symptoms of

[1]Department of Clinical Oncology, St. Elizabeth Cancer Institute, Bratislava, Slovakia, [2]Ist Department of Clinical Oncology, Faculty of Medicine Comenius University, Bratislava, Slovakia, [3]Ist Department of Internal Medicine, Medical Faculty of Comenius University, Bratislava, Slovakia, [4]Slovak Medical University, Bratislava, Slovakia

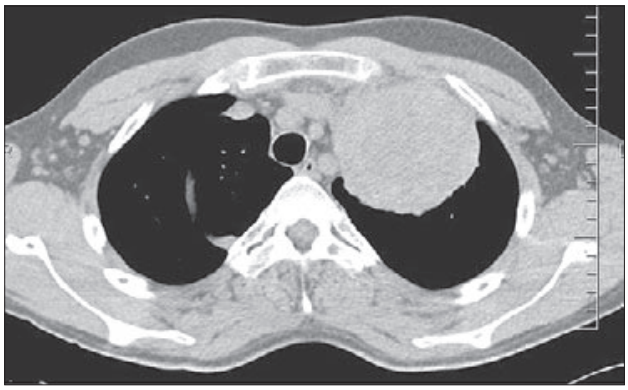
Address for correspondence: B. Vertakova Krakovska, MD, Dept of Clinical Oncology, St. Elizabeth Cancer Institute, Heydukova 10, SK-812 50 Bratislava, Slovakia.
Phone: +421.2.59249274



anemia as a result of a clinically occult blood loss. Blood count showed severe anemia (HGB 68 g/l), the patient was admitted to the hospital for the hemosubstitution. Routine biochemical blood tests showed an elevated erythrocyte sedimentation rate, hypoproteinemia and hypolipidemia. While searching for the cause of a severe anemia, patient underwent various examinations. His stool was tested for the occult bleeding, gastrofibroscopy and colonoscopy were performed, all tests with negative results. Abdomen CT scan with enteroclysis revealed an enlarged small intestine without lymphadenopathy. Due to these findings, the push-enteroscopy was performed. A fragile, bleeding solid tumor of the proximal jejunum with an exulceration, suspected of malignancy, was found (Fig. 1). Samples for pathological examination were obtained. Tissue samples showed extensive malignant cells infiltration. However, due to the small amount of tissue, pathologist was not sure about the precise diagnosis and he could not exclude a rare type of diffuse large B-cell malignant lymphoma. A complete pre-therapeutical staging was performed including a negative CT scan of the thorax and pelvis. CT scan of the abdomen revealed a tumour mass probably arising from proximal jejunum, with infiltrating features and an enlarged paraaortal lymph node (Fig. 2). Based on these findings and due to the patient's status and the risk of ileus and intestinal perforation, the patient was referred for the surgical removal of the lesion. The surgeons performed a palliative jejunal resection with the dissection of paraaortal lymph nodes. Pathology examination with the imunohistochemical staining of the tumour, provided by two independent pathologists, revealed the diagnosis of metastasis of germ cell tumour in the small intestine. The hCG (human choriogonadotropin) serum level was 18-fold higher than the upper normal limit. Based on these data, a scrotal ultrasound examination was performed, disclosing a small pathological mass measuring 1.5 cm in the greatest diameter- not evident at previously performed physical examination. The patient underwent the right radical inguinal orchiectomy. Histological diagnosis of the testicular tumour revealed seminoma combined with teratoma. Based on these results, the patient completed 4 cycles of BEP (Bleomycin, Etoposide, Platinum) chemotherapy experiencing only a mild toxicity and resulting in a complete clinical and biochemical remission according to the RECIST criteria.

Case report 2

On May 2004, a 21-year old man underwent surgery (right inguinal orchiectomy) for a malignant testicular tumor (embryonal carcinoma and teratoma with spontaneous necrosis). Three weeks after the surgery he presented with fever, nausea and a profound short-term memory loss. He also experienced repeated epileptic grand mal seizures with aura and gastrointestinal discomfort. A subsequent screening for bacterial, viral and fungal infection was without pathological findings. HIV status was negative. Cerebrospinal liquor cytology revealed a lymphocytosis (reactive?) with an absence of any malignant cells. MRI showed an area of an extensive signal alteration in hippocampus without any evidence of pathological leptomeningeal enhancement. Because of patient's deteriorating condition, he was given an empirical treatment with intravenous acyclovir administration for a suspected herpes simplex encephalitis. For the history of malignant disease, the patient was consulted in Vienna and Munich – the paraneoplastic limbic encephalitis (PLE) was suspected. A more detailed immunological investigation, including a paraneoplastic antibody screen, revealed the presence of the anti Ma2 antibodies in patient's serum. As the anti Ma2 antibodies are known to have an association with testicular cancer, a search for recurrence was performed (4). The whole body CT scan and serum tumor markers turned out to be normal. In the absence of any direct evidence for relapsing testicular cancer, the onco-urologist recommended the observation. Six months later, a recurrence of testicular cancer was diagnosed. An elevated serum hCG level was detected along with a retroperitoneal lymphadenopathy and pulmonary metastases as seen on the CT scan. The patient was treated with three cycles of BEP (bleomycin, etoposid, platinum) chemotherapy. After the chemotherapy, a partial response was achieved, and the patient was observed for other three



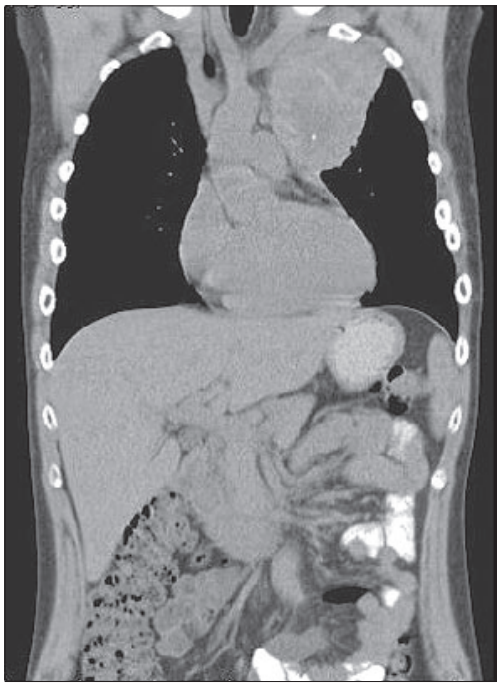
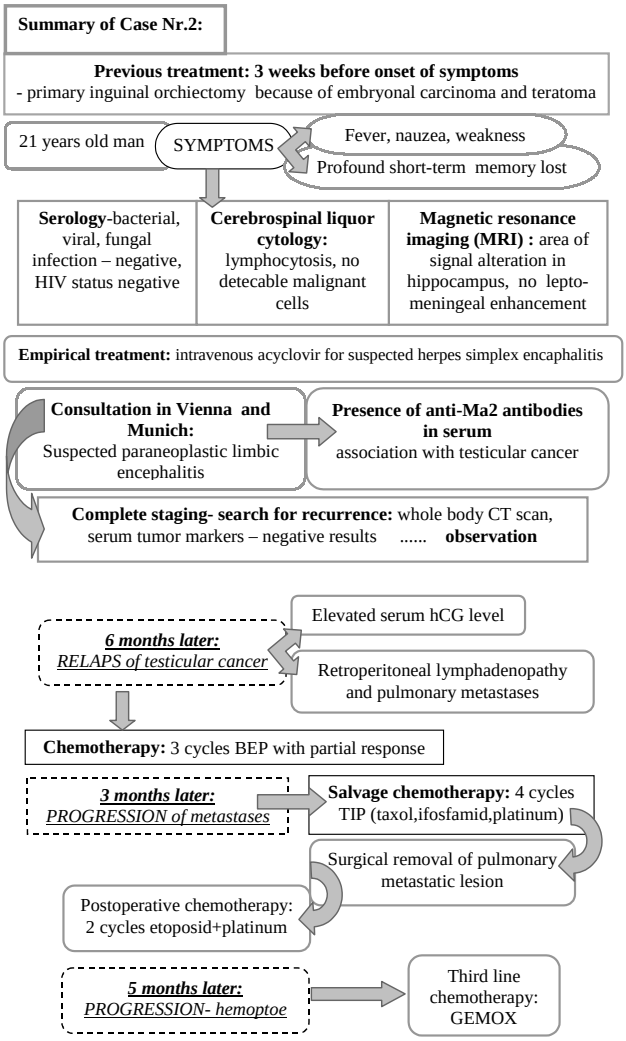


Fig. 3 and 4. Chest CT scan-pulmonary metastatic lesion.



months. A routine CT scan and serum tumor markers showed a progression of pulmonary metastasis and lymphadenopathy. He was treated with the salvage chemotherapy TIP scheme (paclitaxel, ifosfamid, cisplatin) which, after the fourth cycle, resulted in the regression of metastasis. Based on these results, he was referred for the surgical removal of pulmonary metastatic lesion. Morphology and immunoprofile revealed the metastasis of embryonal testicular carcinoma. After the surgery, the patient completed two cycles of postoperative systemic treatment with etoposid and cisplatin leading to the stabilization of the disease. Five months later, the patient presented with a hemoptoe and elevation of serum hCG. CT scan showed a progression of pulmonary metastatic lesion (Figs. 3 and 4). Currently, the patient is treated with the third line of systemic therapy according to the GEMOX scheme (gemcitabin, oxaliplatin) and his condition is stabile, however the neurological status remains with deficit.

Discussion

Testicular tumors are rare, accounting for approximately 1 to 2 % of all tumors (5). It is the most common cancer affecting men in their 3rd and 4th decade. Each year, three to six cases of testicular tumors per 100 000 males are diagnosed (6). The worldwide incidence of germ cell tumors has more than doubled over the past forty years (7). Metastatic disease is detectable at presentation in about 30 % of patients with seminoma and in 50 % of patients with the nonseminoma tumors. Metastases occur mostly in the paraaortal lymph nodes, lungs, liver, bone or brain. Metastases at other sites are less common.

Gastrointestinal bleeding in a young man should lead to the consideration of a testicular cancer in the differential diagnosis. The incidence of gastrointestinal metastases varies with the histological tumor subtype. Nonseminomas more frequently develop gastrointestinal metastases, pure seminomas were only occasionally reported to involve the gastrointestinal tract (5). Involvement of the gastrointestinal tract in metastatic process of germ

cell tumors was described only in few reports. Johnson and colleagues described 26.9 % rate of gastrointestinal metastases found in necropsies of testicular cancer patients. The involved sites were stomach, duodenum, small intestine, caecum, colon and esophagus. The mode of spread to the gastrointestinal tract described in this study was by direct extension from involved paraaortic nodes, hematogenous spread and peritoneal seeding (8, 9). In the report from Chait published in Digestive Diseases in 1978, 25 out of 487 patients with documented gastrointestinal metastases diagnosed postmortem were reported (10). Multimodality approach is required in the treatment of this condition, including emergency surgery (7) as shown in our case, as well. Although these patients often belong to a poor-prognosis group, long-term survival is achievable using the modern treatment principles.

Paraneoplastic limbic encephalitis occurs more frequently in testicular cancer than in other cancer types (11). This rare neurological disorder is characterized by personality changes, irritability, depression, seizures, memory loss and dementia (12). The identification of the anti Ma2 antibodies (antibodies against neuronal proteins) in the serum and liquor of patients with neurological disorder (paraneoplastic syndrome) has uncovered the existence of antigens shared by some tumors and the nervous system (so-called onconeuronal antigens). Paraneoplastic syndromes and enhanced Ma2 level often precede the diagnosis of the tumor by several months or longer (5), and are often more devastating than the cancer itself (11). Patients with neurological symptoms, particularly young men, should be examined for serum antibodies against Ma2 since this marker is indicating the presence of an associated neoplasm. PLE is a well recognized, but poorly understood non-metastatic neurological process. It is characterized by an inflammatory infiltration of the hippocampus as was seen in our second case.

Based on our observations, we conclude that especially in young men, a precise examination of unusual and nonspecific neurological symptoms, and the possibility of malignant germ cell testicular tumor should not be overseen.

References

1. Schmoll H.J. Extragonadal germ cell tumors. http://esmo.org/10.1093/annonc/mdf669. 2002.

2. Plukker JTh, Schraffordt Koops H, Sleijfer D, Oosterhuis W, Van der Jagt E. Intestinal Hemorrhages in Patients With a Nonseminomatous Testicular Tumor. Cancer 1991; 68: 2630—2632.

3. Raghavan D. Germ Cell Tumors. London; BC Decker Inc, 2003: 51—57.

4. Tan PL, Anslow P. Occult testicular cancer presenting as paraneoplastic limbic encephalitis. Clin Radiol Extra 2004; 59 (10): 109—112.

5. Sweetenham JW, Whitehouse MJ, Williams JCH, Mead MG. Involvement of the Gastrointestinal Tract by Metastases From Germ Cell Tumors of the Testis. Cancer 1988; 61: 2566.

6. Laguna MP, Pizzocaro G, Klepp O, Algaba F, Kisbenedeck L, Leiva O. EAU Guidelines on Testicular Cancer. Europ Urol 2001; 40: 102—110.

7. Bosl GJ, Motzer RJ. Testicular Germ-Cell Cancer. New Engl J Med 1997; 337: 242—253.

8. Norda C, Fossaring SD, Giercksky KE. Gastrointestinal Presentation of germ Cell Malignancy. Europ Urol 2000; 38: 721—724.

9. Johnson DE, Appelt G, Samuels ML et al. Metastases from testicular carcinoma: Study of 78 autopsied cases. Urology 1976; 8: 234—239.

10. Chait MM, Kurtz RC, Hajdu SI. Gastrointestinal tract metastasis in patients with germ cell tumor of the testis. Digestive Dis 1978; 23: 925—928.

11. Voltz R, Gultekin SH, Rosenfeld MR, Gerstner E, Eichen J, Posner J, Dalmau J. A Serologic Marker of Paraneoplastic Limbic and Brain-Stem Encephalitis in Patients With Testicular Cancer. Cancer 1999; 340: 1788—1797.

12. Pfister Ch, Vidart A, Lop-Vip S, Hannequin D, Grise P. Assessment of paraneoplastic limbic Encephalitis in Testicular Cancer. Clin Oncol 2003; 15: 219.

Received July 25, 2008.
Accepted October 20, 2008.