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Case report

Aggressive Intestinal Schwannoma Malignum Mimicking Gynecological Pathology – A Case Report

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A B S T R A C T

Primary malignant schwannoma of the small and large intestine is an extremely rare disease. Therefore, we are going to report an aggressive multifocal malignant intestinal schwannoma in a 66-year old female patient, that was primarily diagnosed as the gynecological tumor that, even after the surgical treatment, had a very quickly recurrence. Small intestine tumors may show images similar to an adnexal tumor, so it is difficult to differentiate one from another prior to the surgery. The patient did not suffer from neurofibromatosis type 1 (NF-1), disease that increases occurrence of malignant schwannoma in comparison with general population. These tumors are often diagnosed late, and radical surgical intervention does not guarantee longer survival. After surgical removal of macroscopically visible tumor masses from this patient, tumor formation within one month after the operation had reached the sizes of 83x66 mm and 85x75 mm respectively, with the occurrence of metastases in the liver, and thereafter the patient died. In differential diagnosis of adnexal tumor small intestine tumor has to be considered, especially if nonspecific symptoms are present.

Key words: *malignant, aggressive, schwannoma, gynecologic*

Introduction

Malignant schwannoma is malignant disease that emerges from the mezenhimal cells. Malignant schwannoma belongs to the group of soft tissue sarcomas (STS). The World Health Organization (WHO) introduced the term malignant peripheral nerve sheath tumor (MPNST), and this replaced previous heterogeneous and often confusing terminology of malignant schwannoma, neurilemoma and neurofibrosarcoma[1,2]. Despite the large presence of the soft tissues in human body, the soft tissue sarcomas are rare tumors and make up to 0.7% of all malignant tumors[3]. Digestive system sarcomas (make 2% of all of the sarcomas in adults) are most commonly found in stomach (47%), small intestine (35%), large intestine and rectum (12%) and esophagus (5%)[4]. The most common histological type is leiomyosarcoma (75.1%), while the other types are considerably less common. MPNST makes 1% of all digestive system sarcomas. The incidence of MPNST is 1/100 000 and constitutes 3–12% of the STS[1,5]. More often occur in males (the male to female ratio is 3.8:1)[1]. MPNST may occur on any part of the nervous system, but most commonly is found on body, limbs, head, neck and paravertebral region[6–8]. It may rarely occur in alimentary system, and extremely rarely in esophagus, small and large intestine[4,6,8]. Localization of malignant schwannoma on female reproductive organs is extremely rare. There are only a few cases of ovary or uterus malignant schwannoma reported in relevant literature[9,10]. Frequency of malignant schwannoma among patients with neurofibromatosis type 1 (NF-1) is greater than in general population and is estimated to be 2–5%[11–13].

Case Report

A 66-years old, obese female patient was admitted to the hospital due to severe suprapubic pain. The patient

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was conscious, contactable, and cardiopulmonary compensated. Her regularity was well, with no traces of blood or phlegm. She complained about persistent pressure during urination. She suffered from heart arrhythmia, arterial hypertension, diabetes type 2, chronic obstructive pulmonary disease (COPD), and hyperlipoproteinemia. There was no family history of NF-1 or malignant diseases.

Gynecological clinical exam revealed hardly mobile, palpable mass in lower abdomen, approximately 20 cm in diameter, which reaches her umbilicus. The laboratory test showed elevated CRP 41.9 mg/L. Other results were normal (L 9.78x10^9/L, E 4.9x10^{12}/L, Hb 137 g/L, Htc 0432 L/L, TCR 297x10^9/L, normal urine value). CA125–22 kUI/L. The ultrasound imagining showed the tumor in the abdomen, most probably of gynecological origin. Computed tomography (CT) findings of the abdomen (Figure 1) showed a lobular lesion with heterogeneous structure, 17 cm in diameter, located in the lesser pelvis (Figure 1a), spreading to the central part of the abdomen (Figure 1b), as well as another lesion of a similar characteristics, 7 cm in diameter, left in the abdomen (Figure 1c). The liver was normal size, homogeneous structure, with normal coefficient of absorption, without suspicious changes (Figure 1d). There were no enlarged lymph nodes. The bladder was pushed up.

The patient was transferred to the University Hospital for Tumors for surgical treatment. Prior to the surgery, general surgeons were consulted as possible primary settlement of the tumor might have been the intestine. During the surgical procedure (Figure 2a-d) a tumor, approximately 20 cm in diameter, located in mesentery of ileum was found. The tumor has infiltrated

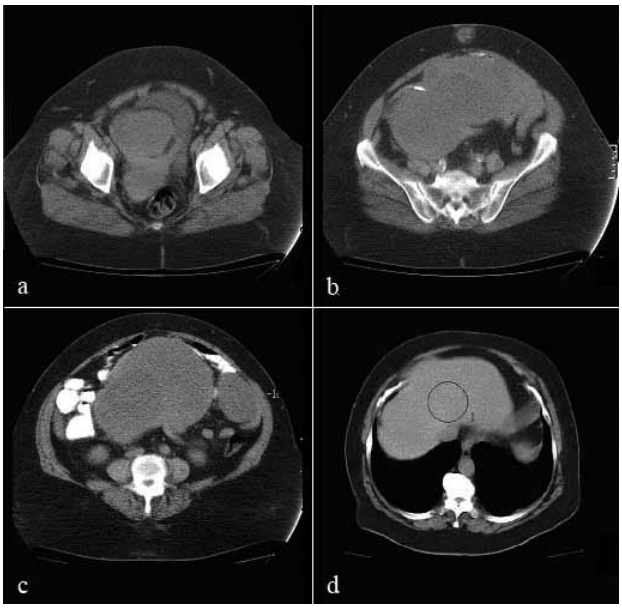

Fig. 1. Computed tomography (CT) findings before surgery a) tumor in the lesser pelvis b) tumor in the central part of abdomen c) tumors occupied the left and central part of the abdomen d) liver without suspicious changes.

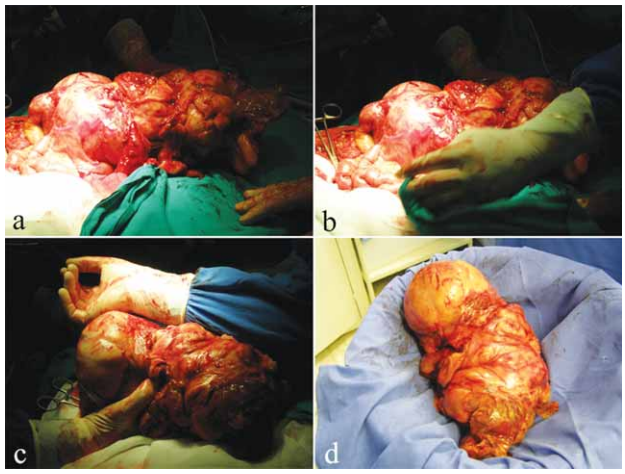

Fig. 2. Surgery a) mobilized tumor mass with small intestine, lateral view b) the tumor located in mesentery of ileum prior to extraction c) rough measuring of the tumor mass d) surgically removed tumor mass.

the ileum and cecum and overlapped the dome of the bladder. The other tumors, approximately 7 cm and 3 cm in diameter, were found in mesentery of jejunum and in mesocolon of descending colon. A few tumor masses of 1 cm were also found on omentum.

The surgical procedure was carried on by the team consisted of general surgeons and gynecologists. All of the described tumors were removed in their entirety, including resection of part of jejunum, resection of ileum and subtotal colectomy and omentectomy. At the end of surgery exploration of abdominal cavity displays normal uterus and both adnexas. The specimens were sent for the pathohistological and immunohistochemical analysis.

The post-operative period passed without any complications. Pathohistological and immunohistochemical anal-

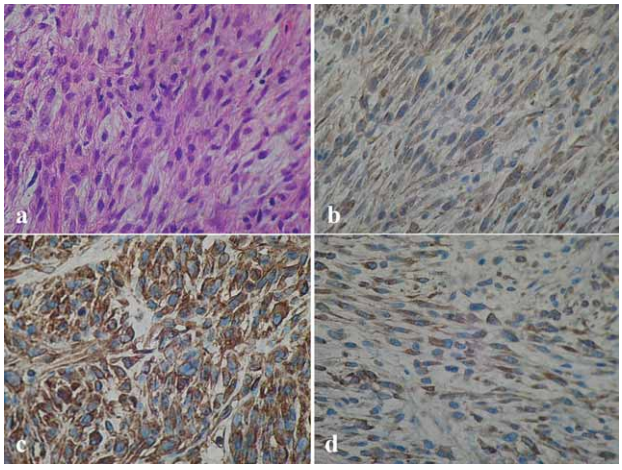

Fig. 3. Immunohistochemical reactions a) hemalaun eosin with pathological mitotic figures (microscopic magnification 200x) b) glial fibrillary acidic protein (GFAP) (microscopic magnification 200x) c) vimentine (VIM) (microscopic magnification 200x) d) neuron-specific enolase (NSE) (microscopic magnification 200x).

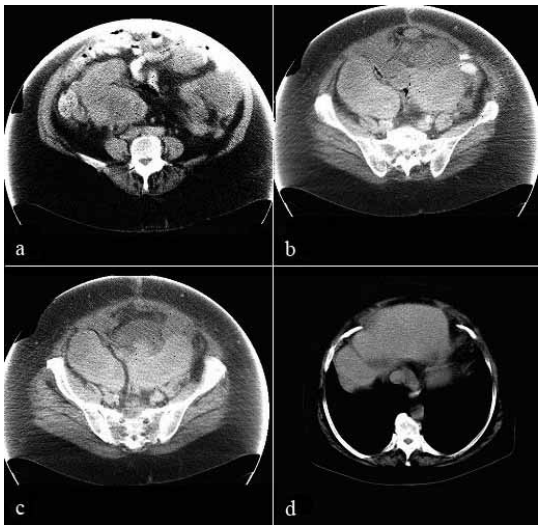

Fig. 4. Computed tomography (CT) findings one month after surgery a) tumors in the abdomen b) tumors extruded between small intestines toward the bottom of the pelvis c) tumors in greater pelvis d) metastasis in the liver.

ysis confirmed the diagnosis of poorly differentiated (high grade) malignant schwannoma, under Coindreu classified as high sarcoma gradus[15]. Histological report revealed that the tumors were composed of elongated spindle cells displaying eosinophilic, partially translucent, light-colored cytoplasm and hyper chromatic nuclei arranged in a storiform pattern. Twelve mitotic figures (Figure 3a) *per* 10 HPF were counted, and there were large foci of necrosis that occupied more than 50% of tumor tissue. Immunohistochemical analysis of tumor cells revealed their positive reaction for glial fibrillary acidic protein (GFAP) (Figure 3b), vimentine (Figure 3c), a focal positive reaction for neuron-specific enolase (NSE) (Figure 3d) and CD 68 (data not shown). Reactions for CD 117 (c-KIT), CD 34, smooth muscle actin (SMA), transverse striated actin, S–100, neurofilament, CD 99, synaptophysin, chromogranin, CD 3, CD 20 and leukocyte common antigen (LCA) were negative.

One month after the operation, during the scheduled check up examination, a recurrent tumor was diagnosed. The ultrasound showed two tumor masses in pelvis: one 83x66 mm, and the other 85x75 mm. CT images of abdomen (Figure 4) showed several spheroid areales extruded between small intestines toward the bottom of the pelvis, pushing up the bladder (Figures 4a-c). The bladder showed no signs of infiltrations, but it seemed that the tumors infiltrated the uterus and adnexas. In the area of 1st segment of the liver close to hilus, the native images showed the hypodense lesion. The post-contrast images showed the focus of secondary deposit (Figure 4d). Based on these findings, this lesion was strongly suspected of being a metastasis. There were several small paraaortic lymph nodes.

The patient was hospitalized two days before starting of the planned chemotherapy, due to severe abdominal pain and signs of cardiopulmonary decompensation. Immediately after hospitalization and 40 days after the surgery, the patient died. Family did not allow the autopsy. The patient, according to hospital documentation, died due to cardiorespiratory failure caused by dissemination of tumor.

Discussion

Observing this case of rare malignant schwannoma of the digestive tract, some of specifics have been noticed. CT and ultrasound examinations displayed gynecological tumor, while surgical intervention has determined digestive system as an exact location. Although all of the tumor masses were removed during the surgical intervention, the ultrasound and CT performed one month later have showed recurrence of the disease. Such a fast development of tumors, which resulted in growth of 83x66 mm and 85x75 mm, is extremely rare. The patient did not suffer from NF-1, the disease in which the frequency of malignant schwannoma is higher in comparison with general population[11,13]. All of these characteristics are rare in general practice, while the combination of them is unique case. Location and size of malignant schwannoma of the digestive tract are most important factors that have an effect on clinical features of this disease. The symptoms are usually non-specific. Cramps or diffuse pain and melena are the most common symptoms of malignant schwannoma of the digestive tract[6]. Palpable tumor is present in 25% of patients[14]. Obstruction of the intestine is often present, although most of the malignant schwannomas grow extraluminal in subserosa[6,15]. The characteristic of these tumors is multifocality, and it means that several primary tumors of same histological structure emerge on different locations[16].

It is impossible to diagnose malignant schwannoma based on symptoms and clinical condition of the patient prior to the surgery. The combination of pathohistological and immunohistochemical analysis of tumor tissue is crucial in diagnosing process, as well as in differentiation from the other soft tissue sarcomas, especially synovial sarcoma, leiomyosarcoma and fibrosarcoma[7,16]. In this case, from the point of histology, possible tumors were: spindle cell sarcoma, gastrointestinal stromal tumor (GIST), gastrointestinal autonomic nerve tumor (GANT), leiomyosarcoma, and primitive neuroectodermal tumor (PNET). The final diagnosis was set after immunohistochemical analysis. The location of tumor, histological picture, positive imunohistochemical reactions for GFAP and VIM (Figures 3b and c), a focal positive reaction for NSE (Figure 3d) and CD 68, negative imunohistochemical reactions for CD 117 (c-KIT), CD 34, SMA, S – 100, neurofilament, CD 99, synaptophysin, chromogranin, CD 3, CD 20, LCA and large number of pathological mitotic figures (Figure 3a) were crucial for final diagnosis of malignant schwannoma and differentiation from other soft tissue sarcomas. All forms of spindle cell sarcoma (spindle cell fibrosarcoma, spindle cell chondrosarcoma, spindle cell sarcomatosis mesothelioma, spindle cell rhabdomiosarcoma, angiosarcoma spindle

cell and spindle cell liposarcoma) were excluded due to tumor localization, histological picture and imunohistochemical reactions in tumor tissue. It is important to note that CD 34 is not specific marker for nerve tumors. CD 34 is used for endothelial and myofibroblastic differentiation of tumors and for evaluation of angiogenesis. Gastric schwannomas are usually positive for GFAP and contain occasional CD 34 positive cells. However, they are negative for CD 117 (c-KIT), desmin and SMA[17].

Diagnosis and treatment of intestinal malignant schwannoma requires a multidisciplinary approach. Radiologists, gynecologists, surgeons, pathologists and internists-oncologists participated in the diagnosis, treatment planning and treatment of our patient.

The treatment is carried out using all three in oncology accepted procedures: the surgical intervention, radiation and chemotherapy, applied individually or in combination. The choice of treatment depends on the clinical stage of disease and level of maturity of cellular elements that form the tumor[18]. Only surgical intervention provides an opportunity for the recovery[7,19]. Intestinal malignant schwannoma poorly responds on radiotherapy and chemotherapy[19]. The accurate diagnosis happens often late[7], which then follows palliative surgical treatment that, in combination with radiotherapy and chemotherapy, in some patients results as an improvement. Remission after chemotherapy has been reported, but without controlled studies[7]. Close postoperative observation is recommended because of the tendency to recurrence and metastasis[7,19].

There are three crucial parameters in determining the degree of malignancy: tumor differentiation, mitotic activity, and degree of tumor necrosis[18]. Histological grading is the most important prognostic factor and the best indicator of metastatic risk in adult STSs. It predicts appearance of distant metastasis as well as overall survival, but not likelihood of recurrence of the local disease[18]. The 5-year survival rate of intestinal malignant schwannoma is unknown[7]. Reviewing the relevant literature we found that only four patients from twenty nine survived 5 years and longest period of survival was 9.5 years[6,20].

Conclusion

The primary intestinal malignant schwannoma is extremely rare[4,20,21]. Based on presented case and all relevant facts, these tumors are usually not diagnosed on time[7,19], while radical surgical intervention does not guarantee longer survival. Tumors of the small intestine may show images similar to an adnexal tumors, so it is difficult to differentiate them prior to surgery[22,23]. Although such cases are so rare, when stating the differential diagnosis of adnexal tumors, possibility of a small intestine tumor should always be kept on mind, especially when non-specific symptoms are present, as well as when is not possible to positively determine the origin of tumor by diagnostic exams.

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AGRESIVNI MALIGNI ŠVANOM CRIJEVA KOJI OPONAŠA GINEKOLOŠKU PATOLOGIJU: PRIKAZ SLUČAJA

S A Ž E T A K

Primarni maligni švanom tankog i debelog crijeva je iznimno rijetka bolest. U ovom slučaju radilo se o multifokalnom malignom švanomu probavnog sustava u 66-godišnje pacijentice, koji je primarno dijagnosticiran kao ginekološki tumor, a nakon provedenog kirurškog liječenja iznimno je brzo recidivirao. Tumori lokalizirani u tankom crijevu mogu dati sliku tumora adneksa i stoga ih je teško preoperativno diferencirati. Pacijentica nije bolovala od neurofibromatoze tipa 1, kod koje je učestalost malignih švanoma višestruko veća nego u općoj populaciji. Dijagnoza ove vrste tumora najčešće se postavlja u uznapredovalom stadiju bolesti, a kirurško liječenje ne jamči duže preživljavanje. Nakon kirurškog uklanjanja makroskopski vidljivih tumorskih masa, tumorske tvorbe su unutar mjesec dana nakon zahvata dosegle veličinu 83x66 mm i 85x75 mm uz pojavu metastaze u jetri, nakon čega je pacijentica preminula. U diferencijalnoj dijagnozi tumora adneksa uvijek treba pomisliti na tumor tankog crijeva, osobito ukoliko su prisutni nespecifični simptomi.