Surgical treatment of neurofibromatosis type I followed by retroperitoneal tumor

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Aim — to determine the optimal surgical approach in patients with abdominal and retroperitoneal manifestations of Recklinghausen’s disease. Material and methods. There were 4 patients (3 women and 1 man) with neurofibromatosis type I who were treated at Vishnevsky National Medical Research Center of Surgery. Results. There were 3 robot-assisted procedures: excision of retroperitoneal tumors (plexiform neurofibroma and schwannoma) in 2 cases and right adrenal pheochromocytoma in 1 patient. We also included 1 clinical case of conventional surgery for neurofibromatosis type I followed by multiple gastrointestinal stromal duodenal and intestinal tumors. In one case, postoperative period was complicated by fluid accumulation in the bed of previously removed tumor that required US-assisted drainage. Postoperative period was uneventful in other cases. Conclusion. Robot-assisted surgery is safe and effective in patients with Recklinghausen’s disease followed by single abdominal and retroperitoneal tumors. It is more expedient to choose conventional technique for multiple tumors located in different parts of retroperitoneal space or abdominal cavity.

Keywords: von Recklinghausen disease, plexiform neurofibroma, schwannoma, pheochromocytoma, gastrointestinal stromal tumor, robot-assisted surgery.

Introduction

Neurofibromatosis type I (Von Recklinghausen’s disease, VRD) is a genetic (autosomal dominant) disease caused by NF1 gene mutation. The most frequent clinical manifestations are pigmented lesion of skin (café au lait macules), Lisch nodules of the iris, as well as multiple benign neurofibromas of the skin and subcutaneous tissue [6, 8, 12, 31]. The incidence of the disease is 1 per 2500—3000 [15, 16]. VRD is rarely associated with neurofibromatous nodes in abdominal cavity and retroperitoneal space [11]. The most common is retroperitoneal plexiform neurofibroma. There are single case reports of association of schwannomas, pheochromocytomas and gastrointestinal stromal tumors (GIST) with neurofibromatosis type I [7, 14, 17]. H. Brems et al. [8] in systematic review reported incidence of GISTs near 6% in patients with neurofibromatosis type I. In most cases, they are represented by multiple intestinal tumors.

Surgery is indicated for pheochromocytoma and GIST. Plexiform neurofibromas and schwannomas are recommended to be removed if they are associated with pain, neurological symptoms and malignant changes [11].

Material and methods

There were 3 robot-assisted procedures for two retroperitoneal tumors (plexiform neurofibroma and schwannoma) and right-sided adrenal pheochromocytoma. We also included one clinical observation of conventional surgery for multiple gastrointestinal stromal tumors of duodenum and small intestine on the background of neurofibromatosis type I.

Clinical observation 1

Patient I., 33 years old, complained of pain in the left gluteal region with irradiation to the left lower extremity, occasional lameness. These symptoms occurred 2 years ago. Outpatient examination confirmed neoplasm of small pelvis and left gluteal region. Biopsy through gluteal access was performed in June 2016 (histological diagnosis — fibromyoma). In July 2016, the patient was referred to the Vishnevsky Institute of Surgery.

Diagnosis of neurofibromatosis type I has been confirmed since childhood (paternal side). There were no concomitant diseases, abdominal and retroperitoneal surgery. Physical examination revealed multiple pigmented lesions of the skin (café au lait macules), multiple intra-
cutaneous and subcutaneous tumor-like formations with maximal diameter near 10 mm. Respiratory, cardiovascular, digestive and urogenital systems were intact. Gluteal area was asymmetric due to increased left half. The right buttock was intact. There was elastic tumor-like painful neoplasm near 12 cm in diameter in the left buttock.

According to contrast-enhanced CT and MRI, multi-nodular retroperitoneal tumor of small pelvis was found. The neoplasm penetrated under small gluteal muscle through the large gluteal orifice. The maximum dimension of the tumor was 12.6 cm. Blood supplying was through superior gluteal artery (Fig. 1).

Considering clinical picture, anamnesis and examination, the following diagnosis was confirmed: neurofibromatosis type I (von Recklinghausen’s disease), retroperitoneal pelvic tumor (neurofibroma) with spreading under small gluteal muscle. It was decided to apply three-stage surgical treatment.

Surgical technique

Superior gluteal artery embolization was performed at the first stage to reduce blood loss (Fig. 2). Duration of endovascular intervention was 25 min.

The second stage included robot-assisted mobilization of retroperitoneal pelvic tumor. Considering pelvic localization of tumor, patient’s cart was placed between patient’s legs to be spread, technical vision console — at the level of patient’s left hip, the assistant was on the right of the patient (Fig. 3).

Abdominal cavity puncture was followed by pneumoperitoneum under 12 mm Hg and laparoscope deployment. Three robotic and 1 assistant trocars were installed under laparoscopic control. Docking was done. Parietal peritoneum was dissected near abdominal aortic bifurcation. Left common, external and internal iliac arteries and left ureter were visualized. Superior pole of the tumor was visualized as soon as left internal iliac artery was mobilized up to its trifurcation. Then we ligated vessels supplying the tumor (those which were previously embolized). Sciatic nerve was also spread on the anterior surface of the tumor. Nerve was precisely mobilized and separated from tumor capsule. Tumor was dissected up to its spread into large sciatic hole by using of bipolar cautery and monopolar scissors. Encapsulated tumor was up to 5 cm in diameter. Peritoneum above the tumor was closed by continuous suture. Robotic stage time was 135 min including docking for about 14 min. The third stage included semilunar incision of the left buttock along superior and medial contour. Aponeurosis of gluteus maximus muscle was open. The muscle was dissected; superior pole of the tumor was visualized. Encapsulated neoplasm was up to 10 cm in diameter, with mellow consistency and spread into small pelvis through a large sciatic orifice. Intact sciatic nerve was placed along the edge of the tumor (Fig. 4). The tumor was dissected and excised by using of monopolar cautery. Tumor bed was drained through counterincision. The wound was closed. Overall duration of the third stage was 105 min.

Total duration of surgery was 265 min, blood loss — 300 ml. According to morphological and immunohistochemical examination, neoplasm was plexiform neurofibroma (S100 expression (polyclonal, DAKO), Ki-67 proliferation index — less than 1%). Postoperative period was complicated by fluid accumulation in the left gluteal area that required US-assisted drainage. Postoperative hospital-stay was 16 days. Patient was discharged in satisfactory condition.

Clinical observation 2

Patient O., 42 years old, complained of constant pain in inferior abdominal area. It was known that the diagno-
sis of neurofibromatosis type I was confirmed at 12 years old. Outpatient examination revealed pelvic tumor. Patient was referred to the Vishnevsky Institute of Surgery to determine further treatment. Concomitant diseases included hypertension, nodular goiter, asthenoneurotic syndrome, multiple Bartholin’s cysts. In 2013 patient underwent partial resection of right optic nerve tumor, in 2005 and 2007 — cesarean section. Physical examination: multiple hyperpigmentation foci throughout the body, tumor-like formations 0.3—4 cm on the back, chest, upper and lower extremities, face. Hypogastrium is slightly painful during palpation. Tumors are not identified during palpation.

Pelvic MRI — neoplasm (most likely neuroma) with a diameter of 75 mm in mesorectal tissue; L₅₋S₇ intervertebral holes enlargement with neuroinomas of spinal roots up to 30 mm (Fig. 5). Following diagnosis was established after examination: Recklinghausen’s disease, retroperitoneal pelvic tumor (neurinoma?), multiple neuroinomas of L₅—S₇ intervertebral orifices, multiple Bartholin’s cysts.

Considering benign tumor, it was preferred robot-assisted removal of pelvic neoplasm which caused pain syndrome.

Pneumoperitoneum 12 mm Hg. Laparoscope was deployed. Three robotic and one assistant trocars were installed under laparoscopic control. Docking of system was done (12 min). Pelvic parietal peritoneum was opened. Dissection and traction of the rectum anterior and upward. Tumor 6×7 cm adjacent to the sacrum by inferior pole was visualized under uterus more to the right. Right fallopian tube was firmly fixed to anterior surface of the tumor. Dissection was associated with high risk of capsule perforation and right-sided salpingectomy was carried out. Tumor dissection was completed by using of mono- and bipolar cautery, ultrasonic scissors. The tumor was placed into Endo Catch pouch. Final hemostasis was followed by pelvic drainage tube deployment. Then transverse mini-laparotomy 4 cm was made in right mesogastrium. The tumor was removed in a pouch. Laparotomy was closed. Surgery time was 245 min, blood loss — 350 ml.

Fig. 2. 1, 2 — Tumor is exposed, robot-assisted dissection of tumor is being performed. 3 — Muscle is exfoliated, superior contour of the tumor is visualized. Neoplasm dimension is up to 10 cm, tumor spreads into pelvis through the large sciatic orifice. 4 — specimen: tumor with marginal areas muscular and adipose tissue.
Fig. 3. MRI-scan of patient O., frontal and sagittal planes. Heterogeneous, solid-cystic, vascularized circular tumor 50×75 mm with clear contours is visualized in mesorectal tissues on the right. Tumor pushes intact rectum to the left and closely adjacent to uterine cervix and posterior vaginal fornix.

Fig. 4. 1, 2 — Stages of robotic dissection of tumor. 3 — specimen: tuberous neoplasm with irregular shape 6×7×5 cm. Uterine tube.
According to morphological and immunohistochemical examination, it was schwannoma (S100 expression [polyclonal, DAKO], Vimentin [V9 clone, DAKO], CD34 [QBEnd/10 clone, Cell Marque], NGFR [MRQ-21 clone, Cell Marque], Ki67 proliferation index less than 1%). Postoperative period was uneventful, postoperative hospital-stay — 7 days. Patient was discharged in satisfactory condition.

Clinical observation 3

Patient B., 37 years old, complained of constantly elevated blood pressure (180/110 mm Hg) with peaks up to 240/200 mm Hg, severe headache. These symptoms occurred 6 years ago. Antihypertensive therapy had no effect. VRD has been diagnosed 4 years before admission to the hospital. There were no comorbidities, previous abdominal and retroperitoneal surgery. Physical examination: skin with multiple pigmented foci. There are tumor-like formations up to 3.5 cm on the back, face, cerebral skull. There are no respiratory, digestive, urogenital diseases. There is an increased level of blood aldosterone up to 580 pg/ml. Blood epinephrine, norepinephrine, angiotsin and urine dopamine are normal. Abdominal CT-imaging confirmed tuberous neoplasm of the right adrenal gland. Prolonged cough and pain in the right hypochondrium, prone to constipation. The diagnosis of neurofibromatosis type I was determined at 17 years old. Pain in the right hypochondrium, nausea and vomiting occurred 1 year ago. Examination confirmed duodenal gastrointestinal stromal tumor with metastatic lesion of right liver lobe. The diagnosis was confirmed by endoscopic biopsy and morphological examination. Three courses of targeted therapy (Sunitinib) were followed by positive effect (reduced dimension of right liver lobe metastasis). Patient was hospitalized to Vishnevsky Institute of Surgery for surgical treatment. There were no previous abdominal and retroperitoneal surgical procedures. Physical examination revealed multiple cutaneous and subcutaneous neurofibromas up to 4 cm, pigmented skin lesions (café au lait macules). Respiratory, digestive, urogenital diseases were absent. CT-imaging: multiple duodenal, jejunal and iliac hypervascular neoplasms up to 84, 18 and 17 mm, respectively (gastrointestinal stromal tumor) (Fig. 6). There were right liver lobe metastases (segments V, VI, VII) up to 7 mm, skin neurofibromatosis.

Robot-assisted surgery was inexpedient due to tumors localization in different parts of abdominal cavity. It was decided to perform distal duodenectomy, tangential jejunal and iliac resection.

Surgical technique

Laparotomy was performed. Palpation did not confirm liver metastases. There was a tumor with bumpy surface up to 12 cm in diameter in the vertical duodenal part. Nodular tumor up to 3 cm was found in lower horizontal part of the duodenum 3 cm distal to previous neoplasm. Similar tumor up to 1 cm was found 15 cm distal to ligament of Treitz. Other 5 tumors up to 0.5 cm in diameter were observed in different intestinal segments. Duodenal mobilization was followed by resection of tumor capsule and mobilization of the ligaments of the right lobe. Posterior parietal peritoneum was opened along inferior vena cava. Mellow adrenal tumor with colorful pattern was placed under inferior vena cava. Inferior vena cava was exposed. The tumor was easily separated from inferior vena cava. Central vein of the adrenal gland flows into posterior wall of inferior vena cava at the level of tumor’s superior pole. Vein was clipped and intersected. The tumor was dissected en bloc without injury of the capsule and removed through mini-laparotomy 5 cm. Tumor bed was drained. Mini-laparotomy was closed. Surgery time was 90 min, blood loss — 100 ml. According to morphological and immunohistochemical examination, it was a right adrenal pheochromocytoma (S100 expression [polyclonal, DAKO], Vimentin [V9 clone, DAKO], CD34 [QBEnd/10 clone, Cell Marque], NGFR [MRQ-21 clone, Cell Marque], Ki67 proliferation index less than 1%). Postoperative period was uneventful, postoperative hospital-stay — 7 days. Patient was discharged in satisfactory condition.

Clinical observation 4

Patient Z., 40 years old, was admitted with complaints of moderate pain in the right hypochondrium, prone to constipation. The diagnosis of neurofibromatosis type I was determined at 17 years old. Pain in the right hypochondrium, nausea and vomiting occurred 1 year ago. Examination confirmed duodenal gastrointestinal stromal tumor with metastatic lesion of right liver lobe. The diagnosis was confirmed by endoscopic biopsy and morphological examination. Three courses of targeted therapy (Sunitinib) were followed by positive effect (reduced dimension of right liver lobe metastasis). Patient was hospitalized to Vishnevsky Institute of Surgery for surgical treatment. There were no previous abdominal and retroperitoneal surgical procedures. Physical examination revealed multiple cutaneous and subcutaneous neurofibromas up to 4 cm, pigmented skin lesions (café au lait macules). Respiratory, digestive, urogenital diseases were absent. CT-imaging: multiple duodenal, jejunal and iliac hypervascular neoplasms up to 84, 18 and 17 mm, respectively (gastrointestinal stromal tumor) (Fig. 6). There were right liver lobe metastases (segments V, VI, VII) up to 7 mm, skin neurofibromatosis.

Robot-assisted surgery was inexpedient due to tumors localization in different parts of abdominal cavity. It was decided to perform distal duodenectomy, tangential jejunal and iliac resection.

Surgical technique

Laparotomy was performed. Palpation did not confirm liver metastases. There was a tumor with bumpy surface up to 12 cm in diameter in the vertical duodenal part. Nodular tumor up to 3 cm was found in lower horizontal part of the duodenum 3 cm distal to previous neoplasm. Similar tumor up to 1 cm was found 15 cm distal to ligament of Treitz. Other 5 tumors up to 0.5 cm in diameter were observed in different intestinal segments. Duodenal mobilization was followed by resection of tumor capsule and
massive bleeding. Complete mobilization of duodenum by Kocher manoeuvre was required to stop bleeding. Tumor pedicle with a diameter near 1 cm was in distal part of duodenum. Duodenum was dissected within 1 cm beyond visible borders of the tumor. The defect was closed by double-row suture. Resection of horizontal part of duodenum was performed to excise the second tumor. The defect was closed by single-row suture. The largest tumor was removed by full-layer resection within 1 cm beyond visible borders of the tumor. Other 5 tumors were excised by the same way. The defects were closed by single-row suture.

Surgery time was 100 min, blood loss — 500 ml. According to morphological and immunohistochemical examination, neoplasms were gastrointestinal tumors (expression of CD117, CD34, alfa-smooth). Postoperative period was uneventful, postoperative hospital-day was 8 days. Patient was discharged in satisfactory condition with prescribed Sunitinib.

**Discussion**

Plexiform neurofibroma (PN) is a neurogenic tumor spreading along the nerves and squeezing surrounding organs and tissues. PN is a relatively frequent manifestation of neurofibromatosis type 1 [30]. Surgical treatment is indicated for PN in view of ineffective medication [21, 24].

We did not find reports devoted to robot-assisted procedures for PN in Recklinghausen’s disease. In 2014, Lei Shi and colleagues reported laparoscopic atypical stomach resection for plexiform neurofibroma localized along greater curvature of the stomach [25]. In our opinion, this clinical example is the first description of robot-assisted surgery for plexiform neurofibroma.

Schwannoma is a benign tumor growing from myelin sheath covering nerve trunks [13]. The most common localizations of schwannoma are head and neck tissues, mediastinum and tissues of the extremities. Retroperitoneal schwannoma is extremely rare (0.5—3%) [17]. There are near 60 cases of surgical treatment of retroperitoneal schwannoma in the literature [20].

Considering development of robot-assisted surgery, we found descriptions of four robot-assisted procedures for schwannoma [5, 17, 20, 29]. However, this tumor was not associated with Recklinghausen’s disease in these reports. In this regard, we can consider our clinical example of robot-assisted surgery for schwannoma (case 2) as the first description of surgical and in particular minimally invasive treatment of schwannoma associated with neurofibromatosis type 1.

![Fig. 6. CT-scan of patient Z., axial and frontal planes, arterial phase.](image-url)
L. Képénékián et al. [18] reported incidence of pheochromocytoma associated with neurofibromatosis type 1 near 0.1—5.7%. There are several case reports of lappochromocytoma associated with neurofibromatosis type 1 [19, 22, 23, 28].

Despite obvious efficacy and safety of robot-assisted adrenalectomy [10], we did not find any publications devoted to robot-assisted adrenalectomy in patients with neurofibromatosis type 1.

Certain relationship between gastrointestinal stromal tumors (GIST) and neurofibromatosis type 1 was described in some articles (case reports and small samples) [7]. In 2016, Toshirou Nishida [27] and colleagues reported retrospective multiple-center cohort study to identify GIST in patients with Recklinghausen’s disease. According to the authors, GISTs are observed in 6.3% of patients with previously diagnosed neurofibromatosis type 1. At the same time, there were no KIT and PDGFRA genes mutations in patients with neurofibromatosis type 1 although they are present in the majority of patients with GISTs. Multiple GISTs are also typical for patients with Recklinghausen’s disease.

Clinical manifestations of Recklinghausen’s disease are presented in Table 1 [11].

Robotic complex is characterized by some well-known advantages: 3D imaging of surgical field, no refraction effect, 7 degrees of freedom of manipulators motion, etc. These factors provide a high level of convenience, safety, precision and ergonomics of robot-assisted operations [1—5, 9, 26, 32]. At the same time, there is a need of intraproductive reinstallation of robotic ports in case of multiple abdominal and retroperitoneal tumors that significantly increases duration and complexity of surgical intervention [1—4].

Robot-assisted surgery is safe and effective for single retroperitoneal and abdominal tumors in patients with Recklinghausen’s disease. Conventional surgery is more advisable for multiple retroperitoneal or abdominal tumors.

No conflict of interests to declare.


