Original Articles

Chirurgia (2013) 108: 26-31
No. 1, January - February

Paraneoplastic Syndrome in Primitive Retroperitoneal Tumours

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Rezumat

Sindromul paraneoplazic în tumorile retroperitoneale primitive

Introducere: Tumorile retroperitoneale reprezintă o patologie neoplazică aparte. Nici o altă patologie umană nu este mai săracă și mai înșelătoare ca și manifestare clinică specifică. Împrumutând de obicei simptomatologia organelor învecinate, tumorile retroperitoneale sunt descoperite cel mai adesea în stadii avansate sau incurabile.
Material și metodă: Vă prezentăm în lucrarea de față dificultatea diagnosticului în 3 cazuri de tumori retroperitoneale primitive, manifestate clinic prin sindromul paraneoplazic. Lotul de studiu a fost compus din pacienți diagnosticați cu tumori retroperitoneale primitive la examenul histopatologic. Majoritatea pacienților au fost selectați din specialități ca urologie sau chirurgie generală, dar am întâlnit cazuri și din alte specialități medicale.
Rezultate: Sindromul paraneoplazic reprezintă secreția unor variate substanțe biologic active de către tumoră. Hormoni, citokine, interleukine, anticorpi, fracțiuni ale complementului sunt doar câteva exemple de molecule active ce pot determina sindromul paraneoplazic. În studiul nostru am întâlnit 3 pacienți din 32 cu acest sindrom. Din istoricul și evoluția pacienților se observă dificultatea diagnosticării acestui tip tumoral.
Concluzii: Fiecare caz în parte a fost o provocare diagnostică, dar și chirurgicală. Sindromul paraneoplazic oferă un plus de dificultate stabilirii diagnosticului final, ceea ce duce de fapt la întârzierea tratamentului. Considerăm că este imperios necesară o colaborare intensă între diverse specialități chirurgicale și medicale pentru stabilirea cât mai precoce a unui diagnostic și tratament adecvate.

Cuvinte cheie: sindrom paraneoplazic, tumori retroperitoneale, semne clinice, substanțe biologic active

Abstract

Introduction: Retroperitoneal tumours represent a particular oncological pathology. No other human pathology is so deceiving and scarce in specific clinical symptoms as these tumours. Usually borrowing the symptoms of nearby organs they are discovered in advanced or incurable stages.
Material and method: We have tried to present to you the challenge of diagnosing some retroperitoneal tumours. One of the rarest signs was by far the paraneoplastic syndrome or the secretion of active biological substances. The study group is composed of histopatologically diagnosed patients. The vast majority were selected from urology and general surgery wards, but there were cases from gynaecology, neurosurgery and even from endocrinology and gastroenterology.
Results: Paraneroplastic syndrome represents the secretion of various substances by the tumour, substances that make changes at bioumoral level. In our study we found 3 cases of 32 patients (9,37%) with paraneoplastic syndrome. What is to be noticed is that because of this syndrome the diagnosis was more difficult and was indirectly referred to a retroperitoneal tumour. We would like to present these cases and their particularities.

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Conclusions: Every case was a surgical and diagnostic challenge. Biologic active substance secretion or the paraneoplastic syndrome makes the clinical picture even more complicated for primitive retroperitoneal tumours. The clinical symptoms of these tumours require a more careful approach of these patients. Close co-operation with other medical specialties in cases such as ours is mandatory.

Key words: paraneoplastic syndrome, retroperitoneal tumours, clinical signs, biologically active substance

Introduction

Retroperitoneal tumours represent a particular oncological pathology. Situated in "no man's land" they present with a great histological diversity that makes them hard to organize into guidelines and therapeutic protocols (1).

No other human pathology is so deceiving and scarce in specific clinical symptoms as these tumors. Usually borrowing the symptoms of nearby organs they are discovered in advanced or incurable stages (2).

They represent a relatively rare oncological pathology, under 0.2% of all tumours. Their incidence is reported between the 4th and 7th decade of life, but they are also to be found at extreme ages (infants and elders). The sex ratio is 1:1 and 70 -80 % are malignant (1,3).

Given the diversity of conjunctive tissue and anatomical elements, retroperitoneal tumours have a vast histological typology (1,2,3,4).

Material and Method

We have tried to present the challenge of diagnosing some retroperitoneal tumours. One of the rarest signs was by far the paraneoplastic syndrome or the secretion of active biological substances (5).

Generally speaking the clinical signs of retroperitoneal tumours are totally deceiving and not specific (*Table 1*). Except for the presence of a palpable tumoural lombo-abdominal mass the other signs and symptoms are borrowed from nearby organs (1,2,6).

The study batch is composed of histopathological diagnosed patients. They were enrolled from many surgical specialties because of their pleomorphic clinical signs. The vast majority were selected from urology and general surgery wards but there were cases from gynaecology, neurosurgery and even from endocrinology and gastroenterology (7).

Retroperitoneal lymphoma (five cases), extragonadal germ cell tumours (two patients with retroperitoneal seminoma) and four cases with secondary retroperitonal tumor (metastasis from renal or genital tumors) were excluded although almost all of them were treated as primitive retroperitoneal tumours (*Table 2*) (7,8).

Basically each and every patient was histopathologically and intraoperatory checked for retroperitoneal organ tumours (9). Imagistics was not considered sufficient as diagnosis criteria from the beginning. Enough biological material (from biopsy, bioptic laparotomy or radical ablation) with peritumoral tissue was prelevated.

Various clinical signs were to be found in this diversity of histopathological types as seen in the chart below. Regarding the paraneoplastic syndrome it appeared in 3 cases (*Fig. 1*).

Without any doubt, proven by numerous clinical studies the best treatment is the surgical one (9,10), large resection margins, in healthy tissue and eventually resection of apparently normal organs if the situation requires.

Table 1. *Retroperitoneal tumours symptomatology*

Signs and symptoms	Clinical expression
Palpable mass	Mostly firm, fixed to nearby tissue, modifies the abdomen symmetry
Pain	Vague, located mostly in flanks
Urologic signs	Renal colic, dysuria, macroscopic haematuria, polakiuria, vesical spasms
Digestive signs	Postprandial fullness, Dyspeptic syndrome, Enema, Constipation, Diarrhoea Hematemesis, Melena, Occlusive and Subocclusive syndromes Icteric syndrome Portal hypertension syndrome with portal or splenic stasis, splenomegalia, esophageal varices, ascites
Neurological signs	Motor and sensitive disorders (paraplegia, areflexia, hypoesthesia, sphincter incontinence caused by cauda equine syndrome)
Vascular signs	Oedema and varices of genital organs and lower limbs (varicocele, vulvocele) with collateral circulation
Febrile syndrome	In tumour necrosis
Hormonal secretion	Hypoglycemic clinical forms of retroperitoneal tumours with insulin – like secreted substances (mesodermal tumours) Arterial hypertension clinical forms (catecholamine secretion as in neuroblastoma) or cortisol or aldosterone (sarcomas)

Table 2. *Primitive retroperitoneal tumour types diagnosed by histopathological exam*

Tumour type	Number of cases
Mesothelioma	1
Fibrosarcoma	7
Malignant Histiocytoma	5
Liposarcoma	10
Leiomyosarcoma	4
Angiosarcoma	2
Haemangiopericytoma	2
Rhabdomyosarcoma	1

Results

Paraneroplastic syndrome represents the secretion of various substances by the tumour, substances that make changes at bioumoral level. Hormones, cytokines, interleukins, anti-

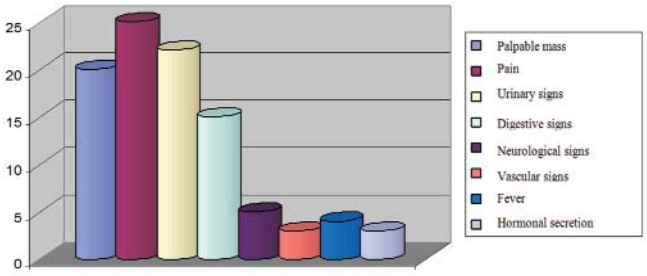

Figure 1. *Clinical signs and symptoms of retroperitoneal tumours in our study group*

bodies, complement system are a few examples of these biologic active substances.

As for primitive retroperitoneal tumours it has been noticed that sometimes mesodermal tumours produce "insulin – like" substances, neuroblastomas produce catecholamines, sarcomas produce cortisol, ACTH, aldosterone.

In our study we found 3 cases of 32 patients (9.37%) with paraneoplastic syndrome. What is to be noticed is that because of this syndrome the diagnosis was more difficult and was indirectly referred to a retroperitoneal tumour. We would like to present you with these cases and their particularities.

Case 1. Male patient, meteorised abdomen (*Fig. 2*), bowel habit changes, elevated transaminase values, modified protein electrophoresis as elevated gamma globulin, intermittent acute renal failure. Clinical and paraclinical investigations established liver cytolysis syndrome with ascites and renal impairment. The abdomen and pelvis CT scan performed in our clinic showed voluminous retroperitoneal mass from diaphragm to the bladder (*Fig. 3*). Radical surgical resection was performed. Macroscopically intraoperatory (*Fig. 4, 5*), what seemed to be retroperitoneal pseudomyxoma proved to be (after further analysis at Babes Institute) myxosarcoma (*Fig. 6*). High levels of normal and modified immunoglobulins were detected in the tumour which explained the intermittent renal failure and the modified protein electrophoresis (*Fig. 7, 8*).

Case 2. Patient admitted in an endocrinology ward for

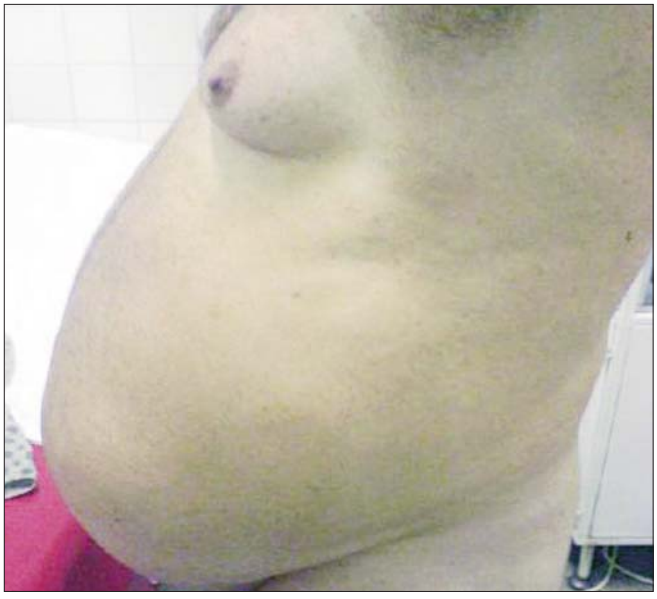

Figure 2. *Clinical image- increased abdominal size due to tumoral mass - case 1*

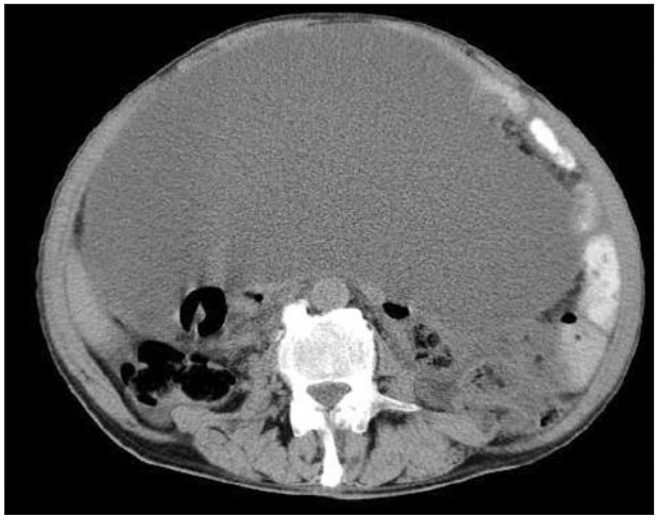

Figure 3. *CT scan showing the giant abdominal tumour – case 1*

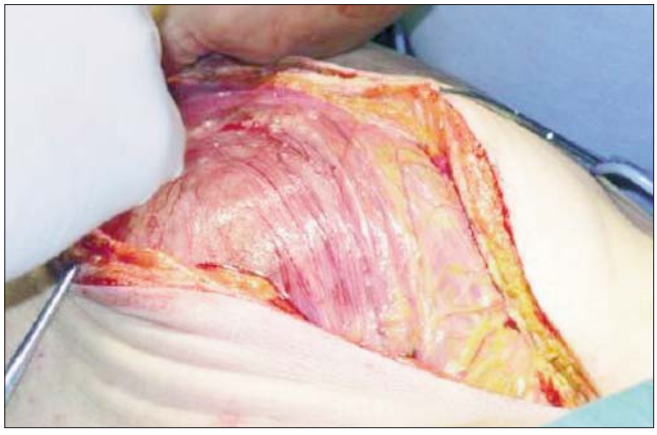

Figure 4. *Intraoperatory image – tumour mass after abdominal wall incision – case 1*

Figure 5. *Intraoperatory images – tumoral content - case 1*

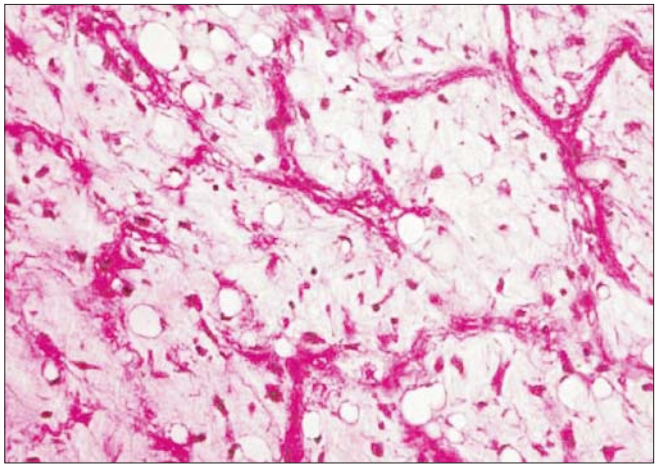

Figure 6. *Microscopic image - Myxoid fibrosarcoma – HE*

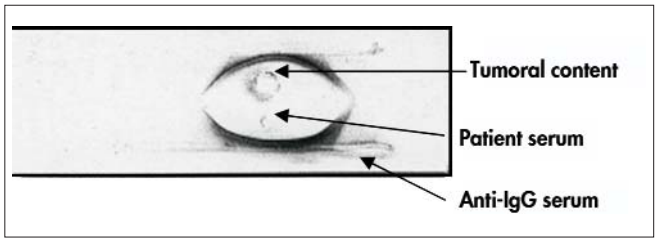

Figure 7. *Modified protein electrophoresis - IgG precipitation arches from tumoral content and patient serum (tumour that secretes immunoglobulines) – Case 1*

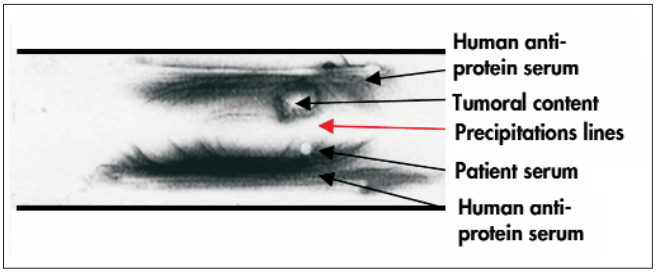

Figure 8. *Modified protein electrophoresis - Precipitations reactions between tumoral content and patient serum (at least three precipitations lines, anti-tumour antibodies) – Case 1*

acute fatigue, tremor and hunger sensation with numerous lipothymia episodes caused by severe hypoglycemia (sugar levels 35 mg/dl). Psychomotor unrest, palpitations, cold sweat (adrenergic answer to hypoglycemia) were always the first signs of hypoglycemic coma. Insulinemia measured in comatose crises reached 300 microunits/ml. Intravenous treatment with 20 % glucose proved to be effective. Insulinoma was ruled out when no pancreatic changes were found on the CT scan. A retroperitoneal mass adherent to the inferior cava was found instead. The patient underwent radical resection of the tumour mass (*Fig. 9, 10*). DNA analysis revealed k-ras gene mutation and deletions of the short arms of chromosomes 11 and 13 similar to MEN 1 gene. The tumour tissue contained somatostatin and insulin

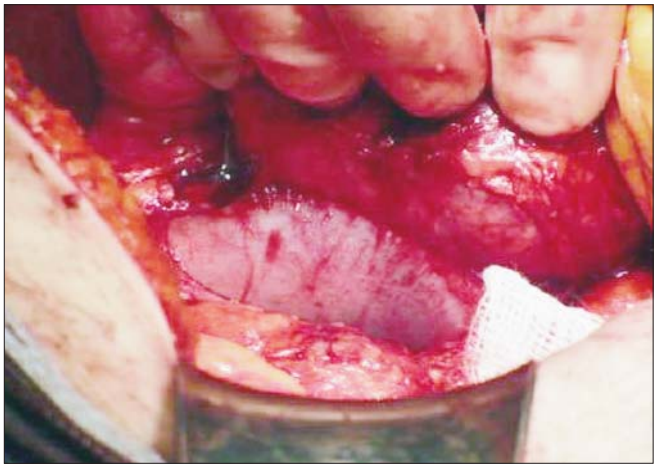

Figure 9. *Tumour adherent to inferior vena cava - Case 2*

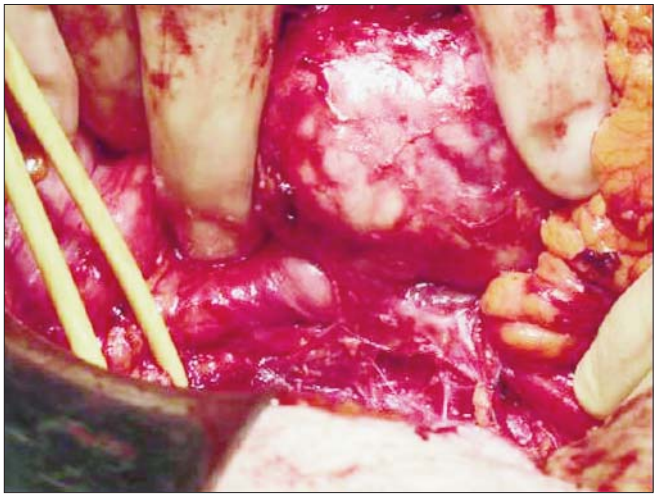

Figure 10. *Dissection of the tumour from inferior vena cava - Case 2*

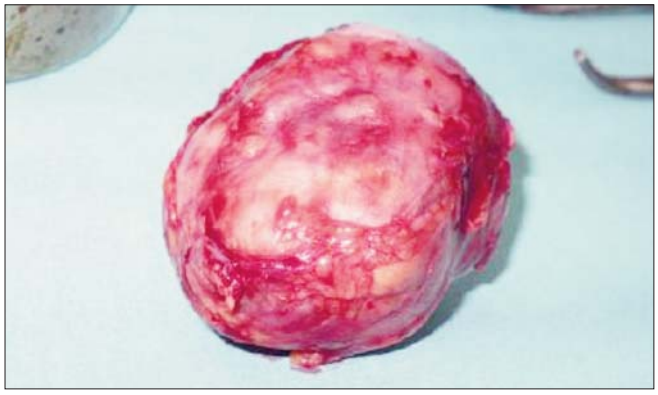

Figure 11. *Macroscopic aspect of excised tumour - Case 2*

– like granules (*Fig. 11, 12*).

Case 3. Female patient signed in an endocrinology ward for Cushing – like syndrome with right hydronephrosis. The patient had arterial hypertension, hirsutism, and cutaneous striae. Dexamethasone suppression test was positive. Only native CT scan could be performed due to contrast substance

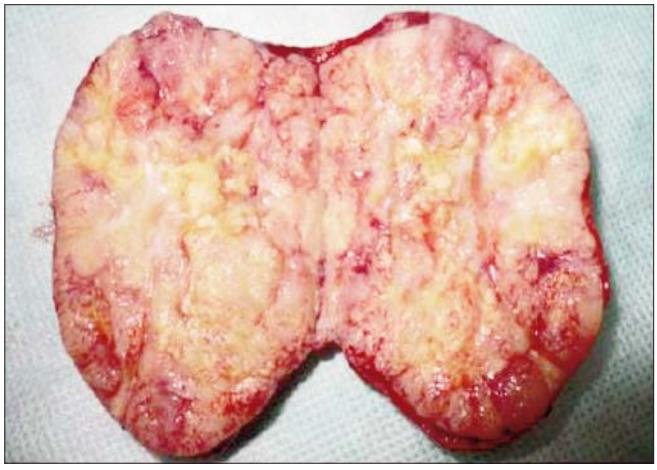

Figure 12. *Longitudinal section of the tumour containing somatostatin and insulin-like granules (bright, whitish spots) – Case 2*

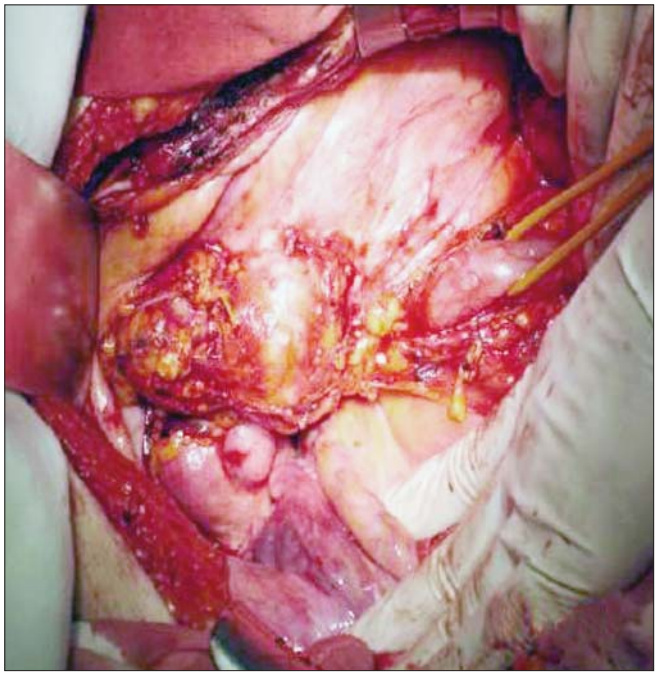

Figure 13. *Dissection and isolation of compressed ureter due to tumoral mass – Case 3*

allergic reaction and it did not reveal any hypophysis, adrenal or thoracic abnormalities. Still a 13/10 cm pelvisubperitoneal tumor compressive on the ureter (secondary ureterohydronephrosys) was found (*Fig. 13, 14*). The ureter was freed from the tumour mass and biopsies were taken. Anaplastic fibrosarcoma was found, the tumour tissue was rich in ACTH (*Fig. 15, 16*).

Conclusions

Paraneoplastic symptoms disappeared in all patients who received surgical treatment. All patients were addressed to an oncologist, 2 of them are now cancer – free and the third

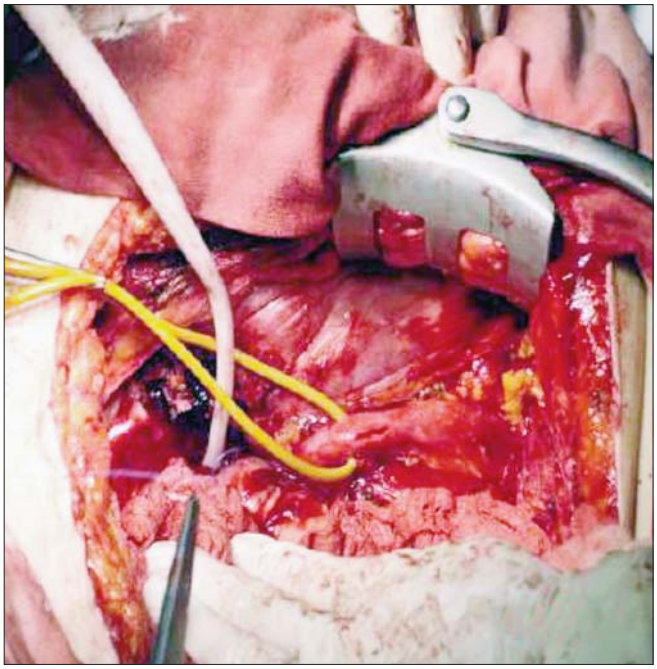

Figure 14. *Ureteral incision and placement of ureteral stent (not showed) – Case 3*

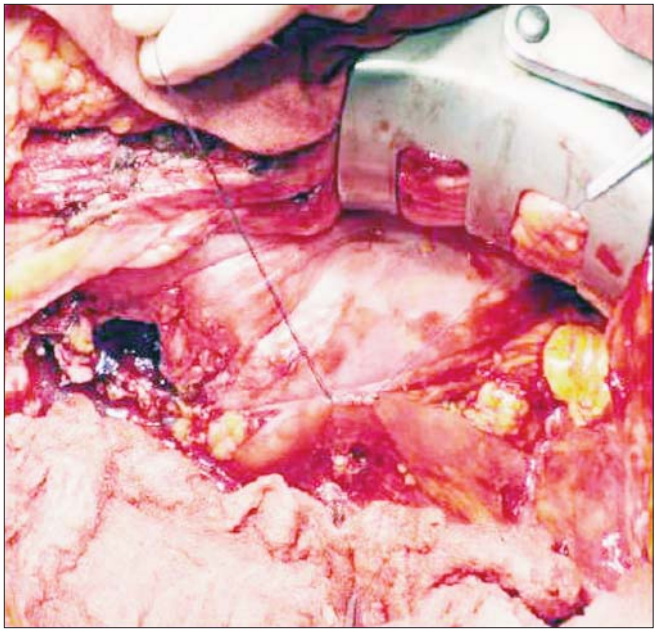

Figure 15. *Ureteral suture after the placement of ureteral stent – Case 3*

patient deceased one year after surgery (11).

Every case was a surgical and diagnostic challenge. Biologic active substance secretion or the paraneoplastic syndrome makes the clinical picture even more complicated for primitive retroperitoneal tumours (6, 12).

The clinical symptoms of these tumours require a more careful approach of these patients. In close co-operation with other medical specialties, as in our cases is mandatory.

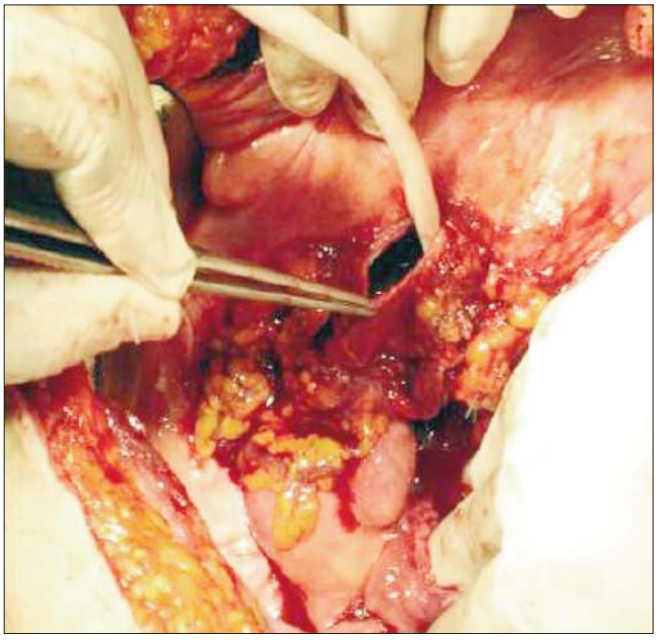

Figure 16. *Clearing of the tumor; tumoral content rich in ACTH – Case 3*

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