„Sf. Spiridon" Emergency Clinical Hospital Iasi
First Surgery Clinic

VON RECKLINGHAUSEN'S DISEASE ASSOCIATED WITH PAPILARY THYROID CARCINOMA AND MALIGNANT MELANOMA WITH MULTIPLE METASTASIS
CASE REPORT

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VON RECKLINGHAUSEN'S DISEASE ASSOCIATED WITH PAPILARY THYROID CARCINOMA AND MALIGNANT MELANOMA WITH MULTIPLE METASTASIS – CASE REPORT –

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Abstract

We present the case of a 56 years old, women, known with Recklinghausen's Disease (RD) since 15 years old. She was in the evidence of Iași Endocrynology Clinic with nodulary goitre since '97, being treated with Euthyrox until 2005. Due to symptomatology worsening (asphyxia feeling, agitation, palpitations, insomnia, irritability, dizziness) and to thyroid increase the surgical procedure was recommended. A right lobeisthmectomy was performed in 2005, but the Histopathology Exam revealed an occult Papillary Thyroid Carcinoma (PTC) pT1NxMxG1 (sclerous infiltrative 3 mm node) on joint nodular goitre with metaplasia, hemorrhage, sclero hyalinisation and lymphomatous thyroiditis aspects. She was treated with L Thyroxin, chemotherapy (Cisplatinum, Dacarbazin) and radioactive iodine therapy. After oncological evaluation she was addressed to the First Surgery Clinic for thyroidectomy totalisation and the treatment of an umbilical tumour occurred after the fourth cure (June-July 2005). The patient was evaluated by physical exam, ultrasonography and computed tomography (cervical and abdominal) which revealed tumours in the cervical region and in the liver. Thyroidectomy totalisation with limphadenectomy and an abdominal laparoscopy and biopsy were performed. The pathologic exam diagnosed multiple metastasis of malignant melanoma (MM) localized in the cervical region, in the liver, great omentum and cervical limphatic nodes. The postoperative follow-up revealed multiple bone mestastasis from the malignanat melanoma. The case particularities were: association of RD with 2 primitive malignant tumours (occult PTC and MM), both diagnosed histopathologically and the multiple bone metastasis developed in a short time.

General information

- S.M. 56 years old, female, from Botosani county
- Admitted to Ist Surgery Clinic St. Spiridon Hospital Iasi (17-31.10.2005)

Reasons for admission:

- Indication of thyroidectomy totalisation
- Occurrence of a round, firmly, badly defined, unpainful tumour of 2 cm in diameter, under the umbilicus.

Anamnesis

insignificant family history:

- mother deceased at age 80-HBP, paralysis by stroke
- father aged 86 –operated on for prostate adenoma 3 years ago
- a brother with High Blood Pressure
- a sister, two sons in apparent health

physiological personal history:

- menarche at age 17 under progesterone treatment
- 4 pregnancies: 2 deliveries (3800, 4850 g), 2 abortions
- irregular and painful menorrhea
- last menorrhea at age 46- surgical menopause

Personal medical history

- **Recklinghausen Neurofibromatosis** diagnosed at age 15
- **Cauterization of pigmentary naevus** at age 17
- 1996 uterine fibromatosis (total hysterectomy with anexectomy)
- 1997 **nodulary goitre**; Chronical Ischemic Cardiopathy. Arrhythmia: ventricular extrasystoles. Tachycardia. Hypertensive Angiopathy. Hypocalcaemia
- 1999 cervical spondylosis
- 2003: High Blood Pressure
- 2004: glaucoma
- 2005: osteoporosis, neurosis related disorder; **occult papillary thyroid cancer; chemotherapy, radioiodine therapy**

Lifestyle conditions: medically retired (worker), non smoker, denies alcohol and coffee intake

History of present illness

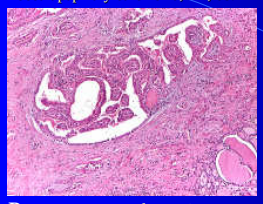
- 56 year old patient, **known with Recklinghausen's Disease (RD) since she was 15** (diagnosed at Iasi Dermathology Clinic) is in the evidence of Iasi Endocrynology Clinic with **nodulary goitre since '97, being treated with Euthyrox until 2005**
- On a reevaluation (21-23.02.2005), due to **symptomatology worsening** (asphyxia feeling, agitation, palpitations, insomnia, irritability, dizziness) and to **thyroid increase** the surgical procedure is recommended, for which she is sent to Ist Surgery Clinic

She is admitted to **Ist Surgery Clinic St Spiridon Iasi** (24.02-8.03.05)

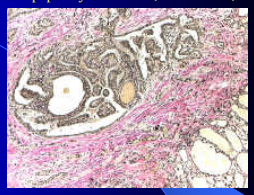
- On the surgical intervention (28.02.05), the intraoperatory macroscopic aspect (nodular, increased Right Thyroid Lobe and normal Left Thyroid Lobe), with technically impossible extemporaneous exam, imposed **right lobeisthmectomy.**
- **Paraphinum Histopathology Exam**:

occult Papillary Thyroid Carcinoma pT1NxMxG1 (sclerous infiltrative 3 mm node) on joint nodular goitre with metaplasia, hemorrhage, sclero hyalinisation and lymphomatous thyroiditis aspects.

occult papillary carcinoma, HE, ob. x 4



occult papillary carcinoma, van Gieson, ob. x 4



- **Postoperatory** the patient was taken over by the endocrinologist who guided her to Oncology for specialty treatment.
- She addresses **Cluj Oncology Institute** on 22.03.05 where she is treated with L Thyroxin, chemotherapy (Cisplatinum, Dacarbazin) and radioactive iodine therapy.
- After oncological evaluation she is addressed to Ist Surgery Clinic for **thyroidectomy totalisation** and **treatment for an under umbilical tumour occurred after the fourth cure** (June-July 2005).

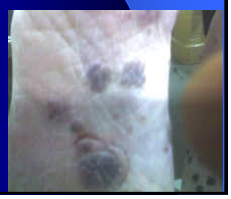
General Physical Exam

Normal except Body Mass Index=30.42, excessive fat tissue

Local Physical Exams:

- Posterior thorax hyper pigmentation with lichenifiation, multiple disseminated hairy pigmentary naevus; diffuse mollusca fibrosa type neurofibromas
- Firmly, badly defined, unpainful 2 cm tumour, localised under the umbilicus.
- At the anterior cervical region, on the right anterior-lateral side there is a palpable, unpainful, 4/3 cm tumour, mobile under the superficial plans

Clinical Exam



Laboratory tests

hyperglycemia (114mg%), **anaemia** (Hb=11,5 g%, Ht=42,3-35,8%), **leucocytosis**, **increased ESR** (35 mm / 1h, 68 / 2 h) **and ALP** (97).

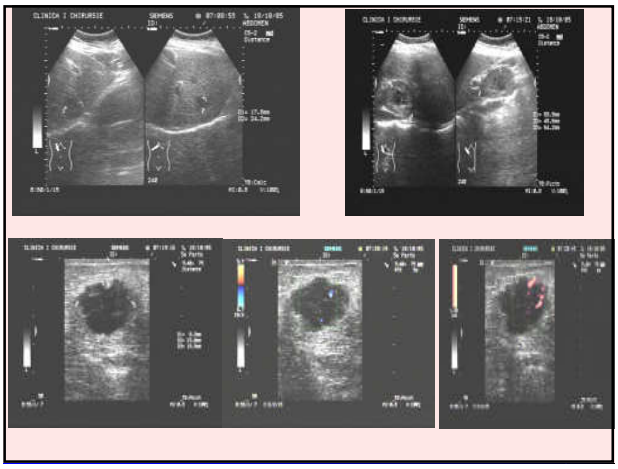
The other are normal: urea, creatinine, AST, ALT, PT, GGT, amilasis, Na, K, Cl, Ca, Mg, Alkaline reserve, PLT, coagulation tests, urinalysis, ECG, chest Xray

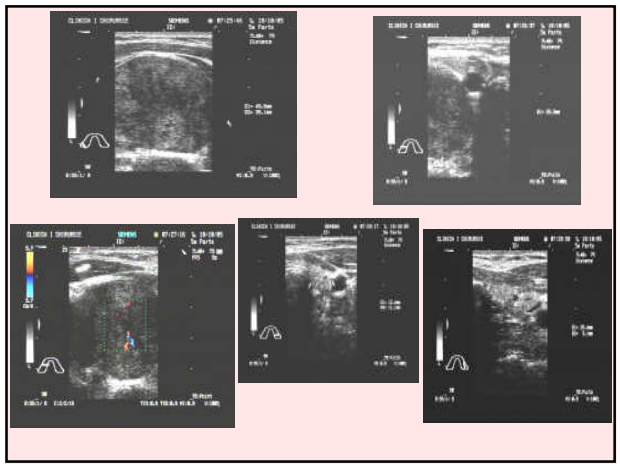
Thyroid Ultrasound:

- No Right Thyroid Lobe.
- Right neck vessels are pushed in front by a **hyperecogenous inhomogenous badly defined, vascularised structure** of 50/35 mm, with liquid areas (adenopathy).
- Small Left Thyroid Lobe (2/11/25 mm); 2 liquid structures
- Absence of left laterocervical adenopathy

Abdominal ultrasound

- **liver** of normal dimension has **a 24 mm formation on segment VI and a 26 mm one in VIII.**
- Under the liver compressing the gall bladder and the right kidney vessels: **a 68/58 mm hyperechogenous formation** with a 23 mm transonic central area.
- **The umbilical tumour** at 8 mm deep: a 23/18 mm wavy surface vascularised inhomogenous- **hyperechogenous formation**





Surgical procedure 21.10.2005

Thyroidectomy totalisation with laterocervical nodes ablation. Surgical protocol

- ✓ **Atypical cervicotomy** to avoid the pigmentary area.
- ✓ Take-off and suspending the muscle-cutaneous structures.
- ✓ Incision of the median raphe: adherence of the sub hyoid muscles which imposed sectioning them.
- ✓ On entering the loge: **absence of right thyroid lobe and isthmus; evidence of a 3 cm structure resembling an adenopathy at vascular-nervous package level**.
- ✓ **Tumour ablation**, sent for **extemporaneous exam**
- ✓ **Presence of a lymphatic cell tissue- removed for paraphinum histopathological exam**
- ✓ LTL macroscopically normal. **Total left lobectomy**. No left adenopathy. Haemostasis control, **Y tube drainage**, skin suture, dressing.

Abdominal time

- **Approach with 3 trocars** of 10 mm, exploration reveals **an under liver 5 cm tumour**.
- **No ultrasound liver metastasis** confirmed.
- **Laparotomy; ablation of the under liver tumour** which resembles an adenopathy and is sent for extemporaneous exam, as well as **a metastatic aspect structure on the great epiploon** and a **3 cm capsulated firm under navel wall formation**. Wall reconstruction, skin suture, dressing.

Postoperatory evolution: surgically favourable

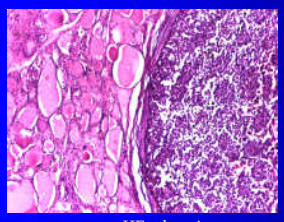
Oncology and endocrinology monitorisation and treatment are recommended

Paraphinum Histopathology Exam:

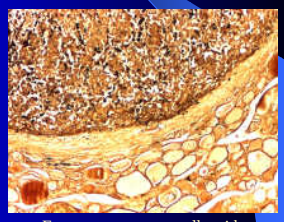
Left Thyroid Lobe

-macroscopically: 2/1.3/0.5 cm

- **microscopically**: **MM metastatic node** with **epithelioid cells, with isolated melanin pigment cells** on a colloid goitre with a hyper functional micro adenoma



HE, ob. x 4



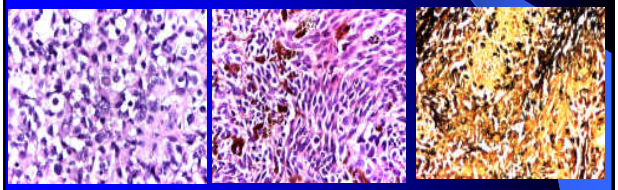
Fontana, numerous cells with melanin pigmentation

Paraphinum Histopathology Exam

	Lateral-cervical adenopathy	Wall abdominal tumour
Extemp	**massive carcinomatous infiltration badly differenced with tubular and papillary differentiation in hotbed**	**diffuse carcinomatous infiltration badly differenced with papillary hotbed and fibrous stroma**
Paraphinum: macroscopically	5/3,7/2,7 cm firm node. Compact whitish and necrotical- haemorrhagic areas	white-grey, compact, defined 3,5/3/2,7 cm node
Paraphinum: microscopically	**lymphatic nodes with total, predominantly epithelioid MM MTS. Broad necrosis areas and isolated melanin loaded cells**	**MM node, the same aspect as the laterocervical nodes**

Paraphinum Histopathology Exam

- **supraclavicular nodes**: intense **MM MTS** in 2 out of 3 nodes
- **great epiploon MTS** : tumour node with **joint MM aspect** (epithelioid and spindle cells) necrosis areas and low melanin pigmentation
- **under liver tumour**: **same aspect**, but intense pigmentation



ob x 20, HE, epithelioid cells type — HE, ob x 10, spindle cells proliferation — Fontana, ob x 10 numerous cells with melanin pigmentation

Discussions
Diagnosis on release:

- **main diagnosis**: **malignant melanoma** with **metastasis**: Under liver tumour, Abdominal parietal tumour, great epiploon MTS, laterocervical Adenopathy, LTL Metastasis; Supraclavicular adenopathy
- **secondary diagnosis**

- Operated occult papillary thyroid carcinoma
- Recklinghausen Neurofibromatosis
- Chemotherapy
- Radioiodine therapy
- first degree obesity

Neurofibromatosis

- **genetical systemic disease** of 8 types with cutaneous, neurological and bony manifestations.
- **The most frequent (85%) is the Ist type: Von Recklinghausen's Disease** described in 1882, with 1/3.000incidence.
- **Clinical manifestations:**
- **cutaneous**: neurofibromas from Schwann cells, fibroblasts, mastocytes and vascular elements; "cafe au lait" spots, ephelides, pruritus)
- **neurological**: tumours, dysfunctions
- **endocryne; ocular:** Lisch nodes; **bony**
- **NF malignisation**

Associated cancers: nephroblastoma, rhabdomyosarcoma, retinoblastoma, malignant melanoma, leukaemia.

RD differential diagnosis:

- the other Neurofibromatosis
- McCune-Albright syndrome ("cafe au lait" spots, precocious puberty, bony symptoms)
- **Carney syndrome** (lentigines, cutaneous and cardiac mixoma, ephelides, hamartomas, pigmentary naevus, endocryne tumours, amyotrophy, obesity, osteoporosis, High blood pressure, deafness, hyperglycemia, mental delay)
- Westerhof syndrome ("cafe au lait" spots, hypo pigmentation, mental delay)
- Bourneville sclerosis
- overlap NF - Noonan syndrome

Treatment: symptomatic, ablation of the NF with malignisation signs, periodical check-ups

Papillary thyroid carcinoma

- **the most frequent TC, the best prognosis**.
- Lymphatic, rarely by blood **metastasis**
- Treated by **total thyroidectomy and cervical lymphadenectomy**, adjuvant methods.
- **The occult types** (under 5 mm) are accidentally discovered during thyroid resection for other diseases (goitre, Basedow)

Malignant melanoma:

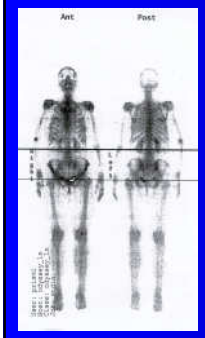
- **Etyology factors**: pre-existent naevus, dysplastic naevus, giant congenital hairy naevus, trauma, UV radiations.
- **Types**: lentiginous, superficial, nodular, acral-lentiginous, unclassified forms.
- Very reserved **prognosis; treatment** by tumour excision.

Postoperatory evolution

On 28.02.the patient has a 3 day old **undermandible formation** (4/5 cm, tough, immobile) and a 2 cm **zygomathic** one and **diffuse bone pain**.

MM will continue to metastasis with fast compression, traction, invasion of near structures.
Possible malignisation of other RD lesions.
Very reserved prognosis. Needs periodical oncology check-up.

Whole body scintigram



Tc99 and Medronate (27.02.06): **multiple bone MTS**:

- **Hyperfixation** in **shoulder joints**, especially the left one where seems to invade the humerus head
- Inhomogeneous **spine** fixation - small zone of moderate hyperfixation on D2
- Hyperfixation on the posterior bow of **right C7 rib**
- Moderate hyperfixation zone: **right sacrum-iliac joint**
- Hyperfixation zone: **left knee**

Now she is in the territorial oncology clinic's evidence.

Case particularities

- **Rarity of RD** occurred probably by **spontaneous mutation** (no RD in the family history)
- **Association of RD with 2 primitive malignant tumours**: occult PTC and MM, only one (MM) constantly associated with RD, both **diagnosed histopathologically**
- The **giant congenital hyper pigmentation** on all posterior thorax
- **Concurrence of no less than 6 MM metastasis**
- After 4 months: 2 more fast growing subcutaneous tumours and **multiple bone MTS**, on a relatively good health state
- **MM evidenced by MTS**

Difficulty of differential diagnosis between nodular metastatic MM, Carney syndrome- 150 cases world wide and melanocyte schwannoma

Conclusions

- Evolution in RD can be long with good general status
- The possibility of **RD occurrence by spontaneous mutation**, of **cutaneous lesions' malignisation**, of **PTC association**
- The **certainty diagnosis** is given by the **Paraphinum Histopathology Exam**
- **Tumour ablation and adjuvant therapy** delay the evolution and increase life quality
- **The need of tight surgeon-oncologist-hystopathologist cooperation** and of careful supervision of the pacients' condition