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Cathepsin-k as a diagnostic marker in the identification of micro-granulomas in Crohn’s disease

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Key words
Cathepsin-k • Crohn’s disease • Granuloma • Immunohistochemistry

Summary
Crohn’s disease is a chronic inflammatory bowel disease, whose aetiology and pathogenesis are still unknown. The occurrence of epithelioid granulomas is one characteristic feature of the disease since these lesions are found in the bowel wall in 50-87% of colectomy specimens. Although granulomas are not pathognomonic, their identification is considered a relevant element for diagnosis. Cathepsin-k, a papain-like cysteine protease, is involved in bone remodelling, and has been widely used as an immunohistochemical marker for the in situ detection of osteoclasts. Interestingly, the expression of this potent protease is also significantly increased in stimulated tissue macrophages, epithelioid cells and granulomas, but is not expressed in resident tissue macrophages. In the present study, we evaluated Cathepsin-k expression as a diagnostic tool in the identification of small granulomas in Crohn’s disease.

Formalin-fixed and paraffin-embedded samples of 10 cases of Crohn’s disease were collected from surgical ileo-colic resections followed by comparison of Cathepsin-k and CD68 immunoreactivity. Granulomas were identified in 4 of 10 cases examined in haematoxylin & eosin preparations. Cathepsin-k enabled the identification of small granulomas (with a diameter between 100 and 200 µm) in 6 of 10 cases, mainly localized within the submucosa and muscular layers. When compared to CD68, Cathepsin-k immunoreactivity was generally absent or only weakly expressed in resting tissue macrophages, thus allowing better identification of activated epithelioid cells.

Based on these results, Cathepsin-k appears to be a reliable tool for the precise and rapid identification of small epithelioid granulomas in Crohn’s disease.

Introduction
Crohn’s disease is a chronic inflammatory bowel disease of unknown aetiology, which is characterized by segmentary involvement of the gastrointestinal tract, cobblestone appearance of the mucosa, and occurrence of epithelioid granulomas in the bowel wall in 50-87% of colectomy specimens 1. The identification of granulomas is not pathognomonic, although their presence is considered a reliable histopathologic element for diagnosis, especially when localised in areas that are distant from ulceration.

In many cases granulomas are very small, consisting only of a few epithelioid cells, which are defined as micro-granulomas 2. Although inter-observer agreement for the detection of epithelioid granulomas is high 3, the occurrence rates vary across cohorts of patients with Crohn’s disease. The availability of a reliable marker for the sensitive detection of micro-granulomas could significantly help in the diagnostic process, but the macrophage markers currently utilized in clinical practice (e.g. CD68, etc.) are not able to distinguish between resident macrophages and activated epithelioid cells.

Cathepsin-k is a papain-like cysteine protease that is expressed at high levels in osteoclasts and is involved in collagen matrix degradation and bone remodelling 4. Interestingly, the expression of this protease is also increased in activated macrophages, epithelioid cells and granulomas 5 6. This suggests that Cathepsin-k can be utilized as a sensitive and specific marker to examine the occurrence of macrophage activation on tissue sections, but information regarding its potential applications in diagnostic pathology remains scarce, and there is no data on its expression in inflammatory bowel diseases.

The aim of this study was to evaluate the expression of Cathepsin-k in tissue samples of Crohn’s disease in order to assess its value as an immunohistochemical marker.

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Material and methods

Tissue samples from 10 cases of ileo-colic resection of patients affected by Crohn’s disease and control cases were retrieved from the files of our Department. Control cases included 5 normal bone marrow biopsies obtained during staging protocol for lymphomas, and 2 sarcoid lymph node samples containing large epithelioid granulomas. All tissues had been fixed in neutral buffered 10% formalin and routinely treated for paraffin embedding. Four-µm thick sections were stained with haematoxylin and eosin (H&E) and immunohistochemistry was performed on subsequent sections, using two monoclonal antibodies specific for Cathepsin-k (clone CK4, Novocastra, Newcastle, UK and clone 3F9, Abcam, Cambridge, UK), and CD68 (Dako, Glostrup, Denmark). Endogenous peroxidase activity was blocked by 3% hydrogen peroxide in methanol for 10 minutes. Heat-induced antigen retrieval for Cathepsin-k was performed using a microwave oven and 0.01 mol/L of citrate buffer, pH 8.0, for 30 min. All samples were processed using a sensitive “Bond polymer Refine” detection system in an automated Bond immunostainer (Vision-Biosystem, Menarini, Florence, Italy). Sections incubated without the primary antibody served as a negative control.

The number of cases in which granulomas were identified in H&E sections were counted, and compared those with immunohistochemical analysis. Moreover, the number of granulomas identified were also counted, and their dimension was quantitatively analyzed using the Aperio System (Aperio Technologies, Inc.; ScanScope OS System) to evaluate the detection sensitivity of morphological analysis on H&E preparations and on Cathepsin-k immunohistochemical preparations.

Results

In bone marrow and sarcoidosis control samples, osteoclasts, epithelioid cells and giant cells showed a strong...
immuno-expression for Cathepsin-k, whereas lymph node sinus macrophages were mostly negative, with the exception of germinal centre macrophages exhibiting moderate immunoreactivity. Similarly, in Crohn’s disease Cathepsin-k expression was seen in epithelioid granulomas. In some cases, Cathepsin-k underlined CD68-negative clusters of spindle myofibroblasts in areas of fibrosis, as previously described. CD68 was expressed in all types of macrophages, including both epithelioid cells, giant cells and background macrophages in all 10 cases. Granulomas were morphologically identified in 4 of 10 cases examined in H&E sections (Fig. 1a and 1c), with an average diameter was 500 μm, and a minimum value of 291 μm. Cathepsin-k enabled the identification of granulomas in 6 of the 10 cases, multinucleated giant cells in 1 case and a greater number of granulomas in almost all cases (Fig.1b, 1d). The smallest granulomas identified by Cathepsin-k immunostaining had a diameter that varied from 100 to 200 μm (Fig. 1e), with an average diameter of 166.2 μm, mainly located within the submucosa and muscular layers. CD68 highlighted all types of macrophages, including epithelioid cells, and allowed the detection of granulomas in 6 of 10 surgical samples (Table 1). The intensity of CD68 expression in granulomas was weaker compared to Cathepsin-k.

Conclusions
Herein, we provide evidence that Cathepsin-k immunostaining allows simple identification of granulomas in surgical samples of patients affected by Crohn’s disease, thus representing a useful diagnostic tool in the identification of small size granulomas (micro-granulomas). It can also aid in detection when distortion artefacts are present in tissue samples. Crohn’s disease is a chronic inflammatory bowel disease characterized by a transmural inflammatory reaction in which granulomas are not always present, but they are an important element of support for diagnosis. Although in early studies Cathepsin-k was only detected in osteoclasts, recent reports have revealed a wider distribution pattern, with strong expression of this potent protease in activated macrophages, including epithelioid cells and giant cells in granulomas, as well as a weaker expression in myofibroblasts at foci of ongoing fibrosis. The molecular mechanisms accounting for Cathepsin-k expression are complex and probably heterogeneous in different systems. In osteoclasts, the expression of Cathepsin-k is dependent on the transcription factor MITF, as in macrophages where Toll-like receptor signalling, via p38, can lead to MITF activation and Cathepsin-k expression. In our study, the immunohistochemical analysis allowed detection of granulomas in 6 of 10 surgical cases. Notably, in 2 cases the diameter was about 100-200 μm and could not be easily recognized by morphology alone. Cathepsin-k, as a marker of activated and epithelioid macrophages, may be useful in the evaluation of colon and rectal biopsies, allowing a better distinction from resident resting macrophages and muciphages and can represent a sensitive and robust marker for rapidly detecting small granulomas and micro-granulomas in samples where Crohn’s disease is suspected.

References
Recurrence of nevoid melanoma originally diagnosed as benign nevus

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Key words
Nevoid melanoma • Recurrence • Diagnosis

Summary
We report the case of a 27 year-old woman who had a pigmented lesion in her left leg in 2004. The lesion, which was diagnosed as a congenital compound nevus, recurred four years later as an obvious melanoma.

Introduction
Nevoid melanoma is one of the most deceptive lesions in dermatopathology. It is an intense area of investigation among pigmented lesions at present, given that atypical Spitz/nevi tumors are well studied and more often observed in practical work with a cautious attitude. Here, we report the case of a 27-year-old woman who had a pigmented lesion in her left leg in 2004. The lesion, which was diagnosed as a congenital compound nevus, recurred four years later as an obvious melanoma.

Case history
A 24-year-old women sought medical attention for a pigmented lesion localized on the left leg. The lesion was surgically removed. The excised cutaneous portion measured 1.9 x 0.9 cm and the lesion was 0.7 cm in diameter, and dark-brown in color with irregular borders. Four years later, the patient was displeased with the scar from the previous intervention and also noticed a new, dark blue lesion less than one centimeter away from the site of the previous lesion. The nodule was clinically interpreted as a thrombus.

For aesthetic reasons the scar was removed, but during intervention it was immediately clear that the nodule was not a thrombus, and therefore it was excised as well.

After diagnosis of melanoma, the patient had a wider re-excision and a sentinel node biopsy procedure was performed. After a 6 month follow-up, the patient is currently free of disease.

We were requested to give a second opinion, and we received all relevant materials: two haematoxylin and eosin (H&E) sections of the first lesion; six H&E of the recurrent lesion plus two paraffin blocks; all H&E slides from re–excision and lymph node sentinel procedures, including sections immunostained with antibody anti-Mart-1. Immunohistochemistry with antibody anti-Ki-67, S-100 protein, Mart-1 and HMB45 was performed using the Ventana System. All but the HMB45 antibody (Cell Marque) were Ventana antibodies.

The first lesion was originally diagnosed as a benign congenital nevus. At the time of diagnosis, the lesion was difficult to diagnose and obtaining a second opinion was considered to be prudent. Although the presence of some worrisome findings suggesting a possible melanoma were noticed, it was interpreted as a benign lesion, which if completed excised would be considered cured. The pigmented lesion showed nests of melanocytes within the epidermis that were not equidistant from one another. They varied in both size and shape, with peculiar silhouettes (Fig. 1). The intradermal lesion, which resembles the intraepidermal component, merged imperceptibly with smaller nevoid cells. There were few
The recurrence was a melanoma with a nevoid component in the papillary dermis with a separate large, spindle cell melanoma deep in the lower dermis (Fig. 3). The latter nodule was characterized by confluent collections of fascicles of spindle cells, which were often heavily pigmented, together with melanophages (Fig. 4). Necrosis was also observed. The neoplastic cells infiltrated the adipose tissue of the hypoderm along the septa, without presence in the lobules. The tumor was Clark level V, with a 12 mm thickness in the vertical growth phase. There were 12 mitoses per square millimeter and tumor lymphocytic infiltrate (TIL) was absent. The re-excision was free of tumor and the sentinel lymph node was histologically negative.

**Discussion**

The term nevoid melanoma was used by Schmoeckel, Castro and Braun-Falco in 1985 to describe primary...
cutaneous malignant melanomas with histological features suggestive of benign nevocytic nevi. They stated that some of the following histological characteristics were always observed: cellular atypia, mitoses, adnexa infiltration in the deeper dermis, infiltrative growth, pigmented tumour cells, sharply demarcated tumour nests and the absence of maturation.

The clinical behaviour of nevoid melanoma does not differ significantly from ordinary melanoma, and tumour thickness was the most important prognostic criterion. Lesions which share similar histological findings were called borderline melanoma by Reed, Clark and Mihm in 1975. In 1985, the group of Mihm initially described this subset of lesions with the term *minimal deviation melanoma*, but in 1995 decided to use the more committal and popular term of *nevoid melanoma*, suggesting that proper attention to cytological detail and subtle architectural features aid in recognizing this unusual variant of malignant melanoma. Similar observations were made by Zembowicz et al.

In the present case, the lesion excised in 2004 was dome shaped and melanocytes showed subtle morphologic irregularity with lack of involutitional changes and presence of mitoses in the middle part of the lesion. Also, possible vascular invasion was found. All these features can be present in an ordinary nevus, but their concomitant presence in a lesion probably gave rise to the suspicion that the lesion could have an aggressive behaviour.

Four years later, the lesion recurred at the site of previous excision. The pattern of recurrence was unusual: the superficial lesion showed a substantial similarity to the lesion removed four years earlier. Separated from the superficial component, there was a nodule localized in the mid and dip-dermis that was composed of malignant melanoma cells that were mostly spindle-shaped, some of which were heavily pigmented. Epithelioid cells were also present along with melanophages. The neoplastic cells were diffusely positive for melanocytic markers, and Ki-67 showed that positive cells were frequent in the superficial nevoid component. In our opinion, the deep nodule was a unusual variant of melanoma that can mimic a cellular blue nevus.

These double components could be interpreted as two different types of metastasis, since there is no evidence of transition between the two lesions. On the other hand, although less probable, the superficial nevoid component could be considered as a remnant of the primary lesion. The patient had a re-excision and lymph node biopsy, and both were histologically negative. After a short six-month follow-up, the patient is free of disease.

Diagnosis is a relatively easy matter after follow-up, but often highly challenging before. This fact is often forgotten when legal action is taken. Recently one of the authors (GC) wrote a published letter to this journal on a case of a pigmented lesion with inverse destiny (a nevoid melanoma that turned out to be a benign nevus) and many comments are also merited in the present case, which is another reminder that caution is a virtue when dealing with problematic cases such as nevoid melanoma. One can pose the question of what the implications might have been for the pathologist if the original case had not been referred.

References


Ultrastructural profile of microcystic meningioma

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Key words
Microcystic meningioma • Vacuoles • Vascular permeability

Summary

Objective. Microcystic meningioma was originally classified as a subtype of meningioma by the World Health Organization classification of brain tumours in 1993, and accounts for 1.6% of intracranial meningiomas. This subtype is a variety of meningioma in which micro- and macro-cysts are diffuse. The morphologic characteristics are well defined, while the histogenetic mechanism that give rise to these patterns remain unclear.

Materials and methods. The authors present an electron microscopic study of an unusual case of fronto-temporal microcystic meningioma, manifesting as history of headache, right paresis and dysphasia in a 73-year-old female. Computer tomography revealed a large hypodense mass in the left fronto-temporal region, with slight contrast enhancement.

Results. Ultrastructural observation showed complex alterations among small vessels and intratumoral capillaries in a background of severe modification in vessel permeability.

Conclusions. This electronic microscopy study documented that growth of the cyst was due not only to accumulation of extracellular fluid, but also to cytolysis consequent to ingressive hydropic degeneration.

Introduction

Microcystic meningioma is characterized by the presence of macro- and microcysts in the lesion. These morphological aspects can be seen in all meningioma subtypes, but have a higher incidence in the meningothelial subtype. Upon a radiological and macroscopic examination, the lesion usually appears hypodense, soft, “white-milk” coloured, and sectioned surfaces appear as cribrous and with freely-flowing extracellular fluid. By light microscopy, macrocysts are gathered in large intercellular diastasized spaces, and microcysts are present in cytoplasmic matrix of meningothelial cells. Microcysts have no specific walls as they are surrounding by meningothelial cells and contain small amounts of amorphous, eosinophilic, extracellular material. These meningothelial cells are well differentiated: by transmission electronic microscopy, they show interdigitations, desmosomes and cytoplasmic intermediate filaments, while by immunohistochemistry, they show positivity for vimentin and EMA. These elements are found in compact areas, and are strictly organized to form differently oriented cordons and girders; among these, intercellular spaces are frequently present with diastasis due to the loss of desmosomes. The cytoplasm of most of these cells is occupied by microvacuoles which progressively become larger and numerous, which often join and change the cellular body into a cyst that tends toward cellular lysis. The vacuoles contain some plasmatic proteins instead of lipids and mucins. The microvacuolization process is more severe in proximity of the vessels and along the tissue fascia that surrounds the macrocysts. Cytolysis after vacuolization leads to centrifugal erosion in existing macrocysts, in addition to new cysts arising from cellular separation and breakages in junctional structures. Regarding these intercellular and intracellular gathering of extracellular fluid, together with cytoplasmic excavation and vacuolization, it has been observed that precapillary arterioles and postcapillary venules are affected by hyalinosis of their wall, while capillaries show endothelial pinocytosis and vacuolization, together with elevated permeability.

Through review of the literature data on microcystic meningiomas, it is emphasized that the histogenetic mechanisms giving rise to macrocysts and microcysts are not as well-known as the morphological details. Therefore, even based upon a single case, an ultrastructural study could be useful to investigate the meningothelial and capillary subcellular characteristics of this lesion to better understand the histogenetic mechanisms giving rise to this meningioma subtype.
Case report

A 73-year-old female was admitted to our department with a history of persistent headache. Upon admission, neurological examination showed progressive right paresis and dysphasia. CT demonstrated a hypodense mass with marked compression of the brain in left fronto-temporal region. Most of the lesion was hypodense, except for the tumour capsule observed after intravenous administration of iodated contrast medium (Fig. 1). MRI imaging showed a tumour with a low intensity on T1 weighted images and homogeneous intensity on T2 weighted images. The T1 weighted images disclosed a slight enhancement after administration of gadolinium (Figs. 2a and 2b). During surgery the tumor was clearly demarcated and separated from the surrounding brain tissue. Following its excision, postoperative neurological symptoms improved markedly.

Materials and methods

Serial cuts of the sample were made, and were investigated by either light microscopy or electron microscopy. For the former, samples were fixed in 10% formalin, diluted with 0.1 M phosphate buffer, pH 7.2, and after sufficient dehydration were embedded in histowax; 5 micron sections were cut and stained with either haematoxylin-eosin, haematoxylin van Gieson’s stain, silver staining according to Gomori, or the Azan-Mallory trichrome method. Fragments for electron microscopy were fixed in Karnovsky’s solution, post-fixed in 1% osmium tetroxide, dehydrated in alcohol and embedded in Epon 812 resin. Semi-fine sections were cut and stained with toluidine blue, after which ultra-fine sections were cut and contrasted with lead citrate and uranyl acetate.

Results

Histological analysis

On minimum magnification, macrocysts diffused in a chaotic manner could be observed, and microcysts were present in the cytoplasm of nearly every cell (Fig. 3).
Macrocyts were often made of amorphic, acidophilic material; they had different sizes and no specific wall, since they were surrounded by meningothelial girders. Cellular layers proximal to microcystic cavities were composed of flat meningothelial cells, whose cytoplasm was involved in severe vacuolization and necrosis due to lysis after vacuolization. This phenomenon induced a progressive centrifugal enlargement in all macrocyts, until their confluence and subsequent fusion between adjacent cysts. The solid part of the neoplasm, situated among the macrocyts, was formed by dense and cohesive cords of well differentiated meningothelial elements: the solid aspect was interrupted by microcenters of cellular lysis and intercellular microcavities that formed new microcyts. Most meningothelial cells showed a cytoplasm that was rich in microvacuoles which to converged to transform the cell in a globular, diaphanous element that tended towards cellular lysis (Fig. 4). Precapillary arterioles and postcapillary venules were interesting since they were often involved in a hyalinosis process of the vessel wall and perivascular stroma; they also showed, in many fields, dissociation or thinning in the media wall, and in some sites they presented a reduced and decentralized lumen due to thickening of the fibrotic wall vessels. A saccular downfall of the wall vessel could be observed where the media wall was reduced.

**Ultrastructural analysis**

Observation by electronic microscopy of meningothelial cells showed that there were well differentiated and equipped with junctional structures, interdigitations and intermediate filaments; additionally, many apparently empty vacuoles could be seen. They were embedded in cytoplasmatic matrix, grew in a centrifugal pattern and were often associated with hydropic degeneration, dilated ergastoplasmatic cisterns, swelling of mitochondria, subtotal loss of ribosomes and enlargement of Golgi bodies (Figs. 5-6) Macrocyts were coated by flattened, lamellar meningothelial cells (Fig. 7); they rested upon layers of meningothelial cells with a rarefied, almost diaphanous cytoplasm (Fig. 8). Capillaries were coated by endothelial cells with a bulging diaphanous cytoplasm containing pinocytotic vacuoles, surrounded by a thin and discontinuous membrane.
These vessels were encased by a sleeve of meningothe- lial cells that appeared swollen, diaphanous and poor in substructures.

**Conclusions**

The morphology of cystic meningioma is well known: it is clear that the micro-macrocysts are filled with extracellular material, that the cellular population is made of well differentiated meningotheelial elements, and that the macro-microcysts are regressive and do not involve proliferation of the neoplasm. While the histogenetic mechanisms that govern these regressive processes are not completely understood, it is established that they are due to the abnormal permeability of small intratumoural vessels. By light microscopy, only vascular thickening due to storage of hyalinous material is observed: this feature is to be considered insufficient to demonstrate the complexity of cystic and regressive processes. Electron microscopy analysis, in contrast, highlighted the vascular alterations that could justify the alterations in vessel permeability. Ultrastructural vessel alterations were usually generalized, and involved not only fenestrated endothelial cells but also small vessels and capillary walls.

Importantly, these ultrastructural observations provide a better understanding of the histogenetic mechanism of development of macrocysts and hydropic degeneration of meningotheelial cells. Macrocysts begin to form as flashpoints of intercellular diastasis. Macrocysts have usually a vessel in the centre and grow by collecting extracellular fluid and by lysis of the cells proximal to their lumen. Thus the cells are involved in a hydropic degeneration process that entails both ergastoplasmic and mitochondrial systems.

**References**

Simultaneous leiomyoma and contralateral smooth muscle hyperplasia of the epididymis: a case report

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Key words
Paratesticular tumors • Epididymis • Leiomyoma • Smooth muscle hyperplasia

Summary
We report a case of a 66-year-old man with a simultaneous leiomyoma and contralateral smooth muscle hyperplasia of the epididymis. The left nodule showed characteristics of a benign leiomyoma consisting in the homogeneous proliferation of smooth muscle with a typical pattern of interlacing fascicles of spindled smooth muscle cells showing no mitotic activity. The right nodule was made up of bundles of smooth muscle, growing in a perivascular and interstitial pattern, without the homogeneous aspect of contralateral leiomyomatous tumours. The latter finding suggested non-neoplastic hyperplasia of the smooth muscle fibres of the epididymis. At 6 months after surgery, ultrasound of the scrotum showed no evidence of recurrent lesions.

Introduction
Epididymal leiomyoma is a rare cause of paratesticular masses (Tab. I).1-5. In most literature reviews, the ratio of leiomyoma to adenomatoid tumour in the epididymis is about 1:9. Up to 39% of cases are bilateral, and the presence of an accompanying hydrocele or hernia is found in up to 21% of patients.6-7. Non-neoplastic interstitial or periductal proliferation of smooth muscle can be confused with epididymal leiomyoma.8. We report a case of leiomyoma of the left epididymis associated with smooth muscle hyperplasia of the contralateral epididymis. To our knowledge, this case represents the first reported in the Western literature.

Case report
A 66-year-old male farm worker showed a hard-elastic nodule of the lower portion of the left testicle that was not painful on palpation, about the size of a hazelnut, which he reported appeared three years earlier. During the last year, the patient noted that it increased in size and that another nodule had appeared in the lower part of the right testicle. Ultrasound examination of the scrotum showed both testicles in place with a normal volume, regular margins, homogeneous echostructure without focal lesions. An ovoid nodule non-homogeneous, with regular margins, of about 1.2x0.9 cm was detected in the tail of left epididymis (Fig. 1a). The tail of right epididymis showed a non-homogeneous area with irregular margins of about 0.7x0.5 cm (Fig. 2a). An accompanying hydrocele or hernia was not found. Both nodules were surgically removed with a longitudinal incision and enucleation of the lesions maintaining the integrity of the head of the epididymis. Macroscopically, the nodule of the left epididymis was roundish in shape, hard-elastic in consistency, apparently encapsulated and measured 1.2x1.0x1.0 cm. The cut surface had a homogeneous, bundled and greishy appearance (Fig. 1b). The nodule of the right epididymis was irregular in shape with poorly defined margins, fibrous and measured 0.7 cm across its greatest diameter (Fig. 2b). Histologically, the left nodule showed benign

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leiomyoma characteristics consisting of homogeneous proliferation of smooth muscle with a typical pattern of interlacing fascicles of spindled smooth muscle cells showing no mitotic activity (Fig. 1c). The results of immunohistochemistry are summarized in Table II. The right nodule was composed of bundles of smooth muscle, growing in a perivascular and interstitial pattern, without the homogeneous aspect of contralateral leiomyomatous tumours (Fig. 2c). The latter finding suggested a non-neoplastic hyperplasia of the smooth muscle fibres of the epididymis. At 6 months following surgery, ultrasound of the scrotum has shown no evidence of recurrent lesions.

Discussion

Epididymal leiomyoma is a relatively rare cause of an intrascrotal mass, and the simultaneous bilateral occurrence is even rarer. Other sites of intrascrotal leiomyoma are the spermatic cord and the testicular tunicae. Leiomyomas have a slow and expansive growth with a clinical manifestation of a non-painful palpable nodule. Histologically, the differential diagnoses includes: a) low-grade leiomyosarcoma; b) angiomyofibroblastoma; c) angiomyoipiloma, and d) smooth muscle hyperplasia of the epididymis (Table III). Well-differentiated (low-grade) leiomyosarcomas are distinguishable from leiomyomas only by virtue of mitotic activity (between 1 and 4 mitoses x 10 high-power fields), atypical mitotic figures, nuclear atypia, focal necrosis and infiltrative growth. Angiomyofibroblastomas are a locally aggressive tumour that most often occurs in the vulva. Recently, a small number of cases of angiomyofibroblastomas occurring in men have been reported in the scrotum and spermatic cord. Angiomyofibroblastomas have characteristic perivascular aggregations of plump, rounded to spindled cells, which sometimes display a whirling pattern. Variable myxoid change is frequently observed in these tumours. Angiomylipomas are composed of three tissue components: 1) mature adipose tissue; 2) convoluted thick-walled blood vessels and 3) sheets and interlacing bundles of smooth muscle with a prominent perivascular arrangement. Immunohistochemically, the smooth muscle cells of angiomylipoma are not only immunoreactive for actin and desmin, but also, unlike leiomyoma, express melan-A and HMB-45.

Non-neoplastic proliferative lesions of smooth muscle in the spermatic cord or epididymis have received very little attention in the literature, and have been described in other body systems as hypertrophy, hyperplasia, or hamartomatous proliferation. Barton et al. reported nine cases of smooth muscle hyperplasia of the epididymis and two cases in both epididymis and spermatic cord, clinically mimicking neoplasia. These lesions represent a non-neoplastic excess of native smooth muscle.

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<td>DakoCytomation</td>
<td>Prediluted</td>
<td>Positive</td>
</tr>
<tr>
<td>H-caldesmon</td>
<td>DakoCytomation</td>
<td>Prediluted</td>
<td>Positive</td>
</tr>
<tr>
<td>S-100</td>
<td>DakoCytomation</td>
<td>Prediluted</td>
<td>Negative</td>
</tr>
<tr>
<td>Melan-A</td>
<td>DakoCytomation</td>
<td>Prediluted</td>
<td>Negative</td>
</tr>
</tbody>
</table>

Fig. 1c. Ultrasound in the tail of left epididymis revealed a non-homogeneous ovoid tumour of about 1.2 cm.

Fig. 1b. The lesion was nodular and well circumscribed (haematoxylin and eosin x 10).

Table II. Antibodies and immunohistochemical results of the benign leiomyoma of the left epididymis.
the pathogenesis of muscular hyperplasia, an obstructive, post-surgical, post-traumatic or post-inflammatory mechanism has been proposed. In our case, the patient had not undergone previous surgery for vasectomy and did not report either trauma or inflammation of the testicles, and was not associated with a hydrocele. Even if the association of the two lesions has not been reported in the rare cases described in literature as bilateral leiomyoma synchronous to the epididymis, it is probable that some of the cases diagnosed as leiomyomas were actually non-tumoural hyperplastic proliferations. Surgical excision of epididymal leiomyoma is curative.

### Tab. III. Differential diagnosis for a leiomyoma of the epididymis.

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Differentiating features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-grade leiomyosarcoma</td>
<td>High mitotic activity, atypical mitotic figures, nuclear atypia, focal necrosis and infiltrative growth</td>
</tr>
<tr>
<td>Angiomyofibroblastoma</td>
<td>Perivascular aggregations of plump, rounded to spindled cells, with whirling pattern. Variable myxoid change</td>
</tr>
<tr>
<td>Angiomyolipoma</td>
<td>HMB-45 and melan-A positivity</td>
</tr>
<tr>
<td>Smooth muscle hyperplasia</td>
<td>Increase of smooth muscle fascicles arranged in a periductal, perivascular, or interstitial pattern and lack of the cohesive, well-circumscribed proliferation of interlacing smooth muscle fascicles</td>
</tr>
</tbody>
</table>
References

Rapidly-growing hemangioma of the testicle clinically simulating an aggressive neoplasm. A case report

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Key words
Vascular tumor • Capillary hemangioma • Testicular neoplasm • Testis

Summary
We present a case of intraparenchymatous capillary-type hemangioma of the testicle in an adult. The patient was a 37-year-old man who showed a rapidly enlarging and palpable mass in left testicle. Radical orchiectomy was performed, and histological examination revealed an unencapsulated lobulated tumour with wide hemorrhagic portions. To our knowledge, the occurrence of rapid enlargement in a testicular hemangioma has not been previously reported, which might be explained by the development of intra-tumoural haemorrhage.

Introduction
Vascular tumours of the testicle are uncommon neoplasms that can mimic germ cell neoplasms on clinical presentation 1. The histological types reported in the literature have included capillary and cavernous hemangioma, histiocytoid hemangioma, hemangiendothelioma and angiosarcoma. Testicular hemangiomas generally occur in infancy and childhood, and are rare in adults 2. We report an unusual case of intraparenchymatous capillary-type hemangioma that arose in the left testicle of a 37-year-old man.

Case report
A 37-year-old man was admitted to our department with a palpable left testicular mass that had appeared in the previous two weeks and had gradually enlarged in size. Pain and history of trauma or infection were not reported. Physical examination evidenced a painless enlarged testicle. Ultrasound examination revealed a round and well-demarcated hypoechoic intraparenchymatous mass that measured 2.3 cm in diameter and was located in the upper half of the left testicle (Fig. 1). Colour Doppler sonography showed increased blood flow within the lesion. A small hydrocele was also observed. Serum tumour markers, such as α-fetoprotein, and human chorionic gonadotropin (b subunit), were negative and other laboratory tests were within normal limits. The patient underwent left orchiectomy, with the presumptive diagnosis of an aggressive germ cell tumour.

The surgical specimen consisted of a 5x4x3 cm testicle with 9 cm spermatic cord. The specimen was fixed
in 4% formaldehyde and routinely processed for histopathologic examination. Sections were stained with haematoxylin and eosin (HE).

Gross examination revealed a well circumscribed intra-testicular solid mass of 2.3x2.1 cm with tan and red cut surface, which was located beneath the tunica albuginea (Fig. 2). The epididymis and the spermatic cord were unremarkable.

Microscopic examination evidenced an ovoid and lobulated tumour composed of small closely-packed capillary-type vessels with an inconspicuous lumina. They were filled with erythrocytes and lined by flat endothelial cells (Fig. 3a; Fig. 3b). Occasional typical mitotic figures were identified, whereas pleomorphism was absent. Although unencapsulated, the tumour was well circumscribed and surrounded by seminiferous tubules with a normal appearance. Wide haemorrhagic areas with hemosiderin-containing macrophages were present at the tumour margins. A capillary-type hemangioma was diagnosed.

**Discussion**

Testicular hemangiomas are rare tumours. In a review of the literature of the past 40 years, only about 25 cases of testicular hemangiomas were identified. Most of these were described in infancy or childhood and only 10 cases were reported in adult patients (age range: 18-75 years)\(^1\)\(^-\)\(^10\). Seven cases were left-sided and three were right-sided. Histologically, six cases were diagnosed as capillary hemangiomas and three were classified as cavernous hemangiomas. In one case, pathological examination revealed a venous hemangioma\(^10\). Clinical presentations included asymptomatic, slow and progressive testicular enlargement or long-standing scrotal pain. In two cases, a small concomitant hydrocele and a second degree varicocele were also present.

In this study, we report an additional case of intraparenchymatous capillary-type hemangioma of the left testicle in an adult. Since the testicle showed a rapid enlargement in size in a two-week period, the intraparenchymatous mass observed at ultrasound examination was strongly suspicious for a malignant neoplasm and was treated with orchiectomy.

At microscopic examination, the finding of a proliferation of small, closely-packed capillaries lined by flat endothelial cells exhibiting a lobular growth pattern with no evidence of cytologic atypia, pointed diagnosis towards a benign vascular tumour. The occurrence of a sudden enlargement in a testicular hemangioma has not been previously reported in the literature and might be explained by the development of wide, intra-tumoural haemorrhage.

Angiosarcoma of the testis, although exceptionally rare, was considered in differential diagnosis. This malignant tumour, however, is composed of endothelial cells exhibiting different degrees of nuclear atypia and mitotic activity, and the neoplastic vessels showes a complex anastomosing growth pattern, usually accompanied by wide necrotic and/or haemorrhagic areas. The literature has documented only five cases of true primitive angi-
rapidly-growing hemangioma of the testicle clinically simulating
Primary amelanotic anorectal melanoma: an uncommon neoplasia with poor prognosis

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Key words
Amelanotic anorectal melanoma

Background. Anorectal melanoma is a rare and aggressive mucosal cancer. There is usually a delay in diagnosis because about 30% of these cancers are amelanotic and are often mistaken for benign conditions. Herein, we report a case of amelanotic anorectal malignant melanoma with an unusual metastatic deposit in the vulva and also review the literature.

Case report. A 67-year-old woman presented with a history of prolapse of an anal tumour. Clinical examination showed a pedunculated and ulcerated amelanotic tumour associated with three other nodules, 1 cm in diameter, localized in the vulval mucosa. A left inguinal node was palpable. Histological examination and immunohistochemical staining of all tumours demonstrated malignant melanoma. Radiological diagnostic procedures revealed no evidence of metastases.

Discussion. Nine cases of amelanotic malignant melanoma have been reported in the literature. The age at diagnosis ranged from 45 to 77 years. Females appear to be far more frequently involved than males (F/M = 7/2). Anorectal melanoma is most common in the rectum, followed by the anal canal. Metastases occur early. Our case is the tenth case of amelanotic anorectal melanoma and probably corresponds to multiple synchronous primary melanomas of the anorectal region and the vulva, with the possibility that one of the lesions is a primary melanoma and the others are satellite lesions. Wide local excision where negative margins can be achieved is the preferred treatment.

Introduction
Anorectal melanoma (AM) is a rare and aggressive mucosal cancer accounting for only 0.2% of all melanomas. There is usually a delay in diagnosis because about 30% of these cancers are amelanotic and are often mistaken for benign conditions such as hemorrhoids or rectal polyps. Therefore, AM is associated with extremely poor prognosis. Owing to its infrequency, the optimal treatment of this disease is not well defined. Surgery remains the mainstay of treatment. Herein, we report a case of amelanotic anorectal melanoma with numerous lymph node metastases and an unusual metastatic deposit in the vulva and behind the vaginal orifice. We further review epidemiology, histopathology, diagnosis, and treatments of this disease in light of the pertinent literature.

Case report
A 67-year-old woman presented to our department with a history of prolapse of an anal tumour with recurrent bleeding and anal pain lasting 5 months. The patient complained also of anorexia, loss of weight and alteration of the general state. Clinical examination showed a pedunculated ulcerated amelanotic tumour that arose from the dentate line and encircled the rectum. The tumour measured 5 cm in greatest diameter, was movable, and elastic to hard on palpation. It was attached by a narrow 1 x 1.5 cm pedicle to the posterior wall of the rectum near the vaginal orifice (Fig. 1). A left inguinal node was palpable. The liver was normal in size and shape. Laboratory analyses revealed anemia and hypoproteinemia. Hematoxylin-eosin-staining of the anorectal tumour showed the proliferation of spindle-shaped and epithelioid neoplastic cells in the stroma of the anal mucosa (Fig. 2. a, b, c). These cells were arranged in clusters and short fascicles and infiltrated the epithelium with cluster aggregation. The stroma was not abundant and contained few histiocytes with full-melanin pigment cytoplasm. Immunohistochemical staining was positive.

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for the melanoma markers PS100, melan A and HMB-45 (Fig. 3 a, b). Biopsies of the lesion near the vaginal orifice also featured cells of a malignant melanoma. No evidence of metastases was shown on chest X-ray or upon computed tomography of the chest, abdomen, and pelvis. According to the staging system of the American Joint Committee on Cancer (AJCC), our case was a stage III anorectal melanoma as it was associated with an inguinal lymph node. Local surgical excision was proposed but refused by the patient.

Discussion

Malignant melanoma of the anorectal region is a rare neoplasm, accounting for only 0.6% of malignant tumours of the region and only 0.2% of all melanomas. The first description of AM is attributed to Moore in 1857. Retrospective analyses of 22 studies by Droesch et al. included 533 patients with AM. Median age at diagnosis was 66 years and 57% of the patients were females. Other investigators found a mean age of 50 years at diagnosis and an equal distribution in both sexes. In a recent review, Hillenbrand et al. report three cases of amelanotic AM and found six other isolated case reports during the last 35 years in the literature. Of these, seven were females and two males. The age at diagnosis ranged from 45 to 77 years (median 62 years). Our case is the tenth case of amelanotic AM reported. Patients usually complain of a sense of fullness in the rectum and rectal hemorrhages. Bleeding results from traumatic ulceration or secondary infection of the lesion as in the present case. Other symptoms include anal pain, pruritus, tenesmus, prolapse, change in bowel habit and diarrhea. The average time interval between the occurrence of first symptoms and confirmed diagnosis of AM is 5 to 6 months.

AM is most common in the rectum, followed by the anal canal and anal verge. Most anorectal mucosal melanomas are believed to arise from the transitional zone of the anal canal, where melanocytes are present in the highest number.
The presence of enlarged firm inguinal nodes or neurological complications such as cord bladder or sciatic neuritis indicates metastatic disease. Dissemination from the dentate line is to the liver, lungs and inguinal nodes. Early metastases occur via blood vessels or lymphatics, and are seen in up to 70% of patients at the time of diagnosis. Vulval melanoma with local postsurgical recurrence including the perianal mucosa has been reported. Thus, it is of interest to determine if this is a metastatic deposit of AM in vulva. Another possibility is that there is a common precipitating factor. In fact, multifocality is one of several basic differences between cutaneous melanoma and mucosal melanoma. In its subclinical state, there are multiple foci of atypical junctional melanocytic hyperplasia. With further malignant transformation, mucosal melanoma develops. The total number of primary melanomas could be large. The urethra, vagina, and anus are commonly involved. Therefore, cystoscopy and proctoscopy should be part of the preoperative evaluation and follow-up in vulval melanoma. Radical or extensive resections, may not guarantee freedom from multiple recurrences as long as any mucosa is left. To our knowledge, our patient is the first case of an association between vulval and amelanotic anorectal melanomas. It may represent multiple synchronous primary melanomas of the anorectal region, the vulva and near the vaginal orifice, with the possibility that one of the lesions is primary melanoma and the others are satellite lesions. 

Multiple radiological diagnostic procedures have been used for diagnosing AM such as computed tomography, magnetic resonance imaging, proctoscopy and endoscopic ultrasound. However, because approximately 30% of AM lack pigmentation, these radiological features may not be specific to all AM. The gold standard for the diagnosis is histopathology. Histologically, primary lesions are characterized by nested and single growth of atypical melanocytes in the surrounding mucosa. A careful search for melanin pigment is needed, and in its absence, immunohistochemistry including markers such as S-100, HMB-45, Melan-A and microphthalmia-associated transcription factor (MiTF) or ultrastructural examination may play a role in establishing diagnosis.

The primary modality of treatment for AM is surgery. However, there has long been a debate regarding the extent of resection necessary to optimally treat this tumour. Historically, radical interventions such as abdominoperineal excision of the rectum (APER) with or without inguinal lymph node dissection were preferred. However, as no stage-specific survival advantage has been seen with APER, later studies have recommended wide local excision (WLE) as the preferred treatment where negative margins can be achieved. Adjuvant therapeutic options such as radiation therapy and chemotherapy have been described, but outcomes have not been reported. Sentinel lymph node mapping allows better surgical excision of the presumed sites of lymphatic dissemination in melanoma. Prophylactic bilateral inguinal lymphadenectomy without clinical evidence of involved lymph nodes should not be performed. In a retrospective study of Pessaux et al. including 40 patients with AM, the 5-year survival rate was 24% for patients with stage I tumours, and 0% for those with stage II or stage III disease. In patients with stage I and stage II disease, there was a significant association between poor survival and duration of symptoms (more than 3 months), inguinal lymph node involvement, tumour stage and presence of amelanotic melanoma. Other investigators speculate that there is no difference in terms of age, time of diagnosis, stage and survival between pigmented and amelanotic AM. In our patient, the long period between the onset of symptoms and diagnosis, the presence of inguinal lymph nodes and the tumour stage were associated with poor prognosis. Primary amelanotic AM is an exceedingly rare neoplasm, but should always be taken into consideration as a differential diagnosis in patients complaining of nonspecific symptoms in the anorectal area. Our case
primary amelanotic anorectal melanoma highlights the importance of a meticulous clinical examination to detect other cutaneous and mucosal localizations since synchronous primary melanomas may be present in the same individual.

References

Unusual cause of intestinal obstruction: Ileal endometriosis

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Key words
Endometriosis • Ileum • Obstruction • Diagnosis

Summary
Endometriosis is a common condition affecting the female genital tract, but involvement of the ileum is very rare. Its symptoms are vague and are similar to other benign and malignant disorders, and radiographic findings lack specificity. We report the case of a 23-year-old woman presenting with acute intestinal obstruction for whom preoperative diagnosis favoured acute appendicitis. Laparotomy revealed ileal stenosis. A partial small bowel resection was performed. Pathological examination diagnosed ileal endometriosis. Endometriosis may be a cause of acute abdominal pain in women, and should be considered in differential diagnosis. Difficulties in establishing its diagnosis are discussed.

Introduction
Endometriosis is a relatively common condition that primarily affects young menstruating women, and gastrointestinal involvement in endometriosis has been found at surgery in approximately 12% of patients. Its exclusive location on the ileum is very rare. Correct preoperative diagnosis of endometriosis of the ileum is very infrequent giving the lack of specificity of its clinical and radiologic presentation. We describe a new case of endometriosis that mimicked acute appendicitis and review the clinical and radiologic findings, diagnostic pitfalls and treatment of this unusual lesion.

Case report
A 23-year-old-nulliparous woman, with no previous medical record, presented to the surgical emergency unit for an acute occlusive syndrome following a seven-day history of intermittent abdominal pain with nausea and vomiting. She had no gastrointestinal bleeding or recent weight loss. On physical examination, she had diffuse abdominal tenderness without any palpable mass. Gynaecological examination was normal. Laboratory values were unremarkable (blood sedimentation rate, serum urea, glycaemia, electrolytes) except for a white blood cells count of 14,100/mm³. Abdominal x-rays showed distended loops of small bowel and minimal gas in the large bowel. Acute mesoceliac appendicitis was suspected. Exploratory laparotomy revealed a medium quantity of peritoneal effusion yellow-coloured and an ileal stenosis localised at 25 cm from the ileocaecal valve. The remaining of the bowel and the appendix were normal. Resection of the involved ileum with primary anastomosis and an appendicectomy were performed. The recovery was uneventful. Gross examination revealed the following: the resection specimen consisted of 12 cm of ileum. A stenosis measuring 1 cm with a focal thickening measuring 3 cm was found within the wall of the ileum. The underlying mucosa seemed normal. The serosa was congested (Fig. 1). Histopathological examination of the stenosis and thickened area showed ectopic endometrial glands and stroma within the serosa and the muscularis propria which was enlarged and fibrous (Figs. 2 and 3). There were no signs of malignancy or inflammatory bowel disease. Currently, the patient is asymptomatic without any genital endometriosis after 5 months-follow up.

Discussion
Endometriosis is a common disease of unknown cause that is defined as the presence of endometriotic tissue outside the uterus affecting 5-20% of women. Nul-
liparous women between 20 and 45 years of age are most likely to be affected. The most commonly accepted hypothesis is that endometriotic tissue refluxes through the fallopian tubes during menstruation and becomes implanted on the serosal surfaces of abdominal and pelvic organs. Alternatively, extraterine growth of endometriotic tissue could occur as a result of metaplastic transformation of pluripotential peritoneal mesothelium. Of the extrapelvic sites, the most common is the gastrointestinal tract which is reported in 3 to 37% of individuals with endometriosis. The sites most often affected are the sigmoid colon and rectum, followed in frequency by the appendix and ileum. Ileal endometriosis is generally asymptomatic and incidentally found during abdominal surgery. It can sometimes present with abdominal pain, nausea and vomiting, diarrhoea, gastrointestinal bleeding or signs of acute or chronic intestinal obstruction. The morphogenetic mechanisms linked with intestinal occlusion can be summarized as follows: mural pseudotumoral bulkiness, desmoplastic retraction of the intestinal wall, adhesive enteritis and occlusive endometrial cyst(s). These non-specific abdominal symptoms may suggest diagnosis in case of a cyclic association with menses. Radiologic and endoscopic findings are also disconcerting and have not been well documented in the literature. In a study of five cases, Scarmato et al. concluded that ileal endometriosis may manifest on barium studies as an extrinsic mass effect, as annular...
or as plaque-like lesions. Other radiologic explorations, such as ultrasonography and computed tomography, can show an abdominal mass. Therefore, clinical and radiologic symptomatology of ileal endometriosis often pose problems to the surgeon in the differential diagnosis with other pathologies such as appendicitis, diverticulitis, inflammatory bowel disease and abdominal neoplasms. Moreover, diagnosis of endometriosis during explorative surgery is difficult.

Our patient presented with a clinical pattern of an acute appendicitis. The pathological confirmation was provided by histological diagnosis of the endoscopic and operative specimens. Macroscopic examination showed small superficial nodules or a thickening of the ileal wall with a luminal stenosis. On histological examination, the lesion was composed of endometrial glands and stroma. It was deeply located in the bowel wall. Serosa and muscularis propria are usually involved whereas mucosal involvement is rarely encountered. In the muscularis propria, endometriosis causes muscular hypertrophy and fibrotic reaction causing stenosis. When diagnosis of ileal endometriosis is established, patients may be treated medically with drugs such as Gn-RH analogues, danazol and progestin. The therapy reduces pain, but has no effect on digestive disorders related with stenosis.

Surgical resection of the involved bowel remains the treatment of choice in case of obstruction. Neoplastic transformation can rarely supervene in these endometriotic foci, usually in the form of endometrioid adenocarcinoma, but also sarcomas and Müllerian adenosarcomas.

References

CASE REPORT

Atypical clinical appearance and localization of trichilemmoma. A case report

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Key words
Trichilemmoma • Neoplasm • Cowden syndrome

Summary
Trichilemmoma is a benign cutaneous tumor that shows characteristics of differentiation similar to the outer hair sheath. We report the case of a woman presenting with a nodular tender mass of the back that was diagnosed as an isolated trichilemmoma. Several lines of evidence suggest that trichilemmoma should be considered in the differential diagnosis of any indistinct facial papule. This report documents a non-facial example of trichilemmoma. Atypical clinical appearance and localization of this neoplasm in our patient suggest that only histological findings are specific of this tumor.

Trichilemmoma is a benign cutaneous tumor that shows characteristics of differentiation similar to the outer hair sheath. About 50 articles related to this neoplasm have been published in the medical literature 1. Multiple trichilemmomas are a hallmark of Cowden’s disease. The usual site of occurrence is the face, including the nose and eyelid. We report the case of a woman presenting with a nodular tender mass of the back that was diagnosed as an isolated trichilemmoma. A 52-year-old woman presented to our department with a 5-year history of a slowly enlarging, painful mass on the back. Cutaneous examination revealed a 4-mm high, 1.5 cm diameter, well demarcated, rubbery firm, tender, skin-coloured, nodular mass on the back (Fig. 1). Physical examination revealed no other suspect lesions and no adenopathy. The lesion was surgically excised. Histopathological evaluation showed lobules arising from the epidermis and extended into the dermis with anastomosing islands. Most tumour cells were clear cells with a glycogen-rich content. The outermost cells in the tumor nests were columnar and in a palisading nuclear arrangement with well-formed basement membranes (Fig 2/a). Foci of epidermal keratinization with formation of squamous eddies were observed (Fig. 2/b). These histopathological findings were suggestive of trichilemmoma. The patient did not show any signs of Cowden syndrome. After a follow-up period of 6 months, no evidence of recurrence was observed.

Discussion
Trichilemmoma has been described as a benign neoplasm with differentiation towards pilosebaceous follicular epithelium. Unlike isolated trichilemmomas, multiple trichilemmomas associated with Cowden disease are very rare 2. Trichilemmomas may occur in any race and have no gender preference. They predominantly occur in adults (patients aged 20-80 years), but can be seen as early as 4 years of age. Clinically, the tumor presents as a solitary or multiple smooth, asymptomatic papules or...
verruoid growths. These dome-shaped, flesh-colored lesions are usually shorter than 5 mm in diameter. They often mimic a basal cell carcinoma or a wart. In this case report, the tumor was larger, nodular and the surface was tender mimicking a dermatofibroma. Trichilemmoma most commonly develops on the face, nose, eyelids, lips, and within the oral cavity. A search through literature for the last 30 years failed to identify any report of solitary trichilemmoma of the trunk. In fact, this suggests that this neoplasm has no specific clinical appearance, and may involve any site.

Histologically, trichilemmomas are characterized as sharply circumscribed, lobular epithelial proliferations in continuity with the epidermis, which exhibit a prominent, clear cell component. Other features are peripheral nuclear palisading, a thickened basement membrane, and varying degrees of hyperkeratosis and parakeratosis. Central follicular structures are often present. Desmoplastic trichilemmoma is considered a histologic variant of the trichilemmoma. The underlying cause of trichilemmomas is unknown. Rohwedder et al. demonstrated, for the first time, the presence of HPV DNA in trichilemmomas. Demodex folliculorum is also potentially involved in the pathology of trichilemmoma. This neoplasm may differentiate mainly towards two directions: infundibular keratinization and proliferation of the outer root sheath with undifferentiated and pluripotent characteristics.

Several treatment options are reported, ranging from simple surgical excision to carbon dioxide laser tissue ablation. Carbon dioxide laser is particularly useful if patients have multiple tricholemmomas.

Overall, several lines of evidence suggest that trichilemmoma should be considered in the differential diagnosis of any indistinct facial papule. This report documents a non-facial example of trichilemmoma. Atypical clinical appearance and localization of this neoplasm in our patient suggest that only histological findings are specific of this tumor.

References