

Neoplastic degeneration of chronic sacrococcygeal pilonidal sinus: report of seven cases and literature review

Degeneración neoplásica de sinus pilonidal sacrococcígeo crónico: presentación de siete casos y revisión de la literatura

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Abstract

Introduction: Neoplastic degeneration is an uncommon but extremely serious complication of pilonidal sinus (PS) disease. We pretend to determine the factors that influence in the prognosis of the neoplastic disease assessing clinical features and histological findings. **Materials and methods:** We retrospectively studied the patients diagnosed of malignization of PS in our institution from 2000 to 2019. **Results:** Seven male patients with a mean age at diagnosis of 64.8 years old were collected. Average time between the initial symptoms of PS disease and the tumor diagnosis was 33.7 years. The patients presenting an ulcerative pattern in the primary tumor showed in all the cases perineural invasion, local deep structures infiltration, and neoplastic dissemination to the regional lymph nodes. All these patients died in an average time of 7 months. On the other hand, patients with exophytic patterns in the primary tumor did not present local invasion or regional nodes affectation. All the cases survive with an average follow-up of 70.5 months. **Conclusions:** Ulcerated lesions clearly show a worse prognosis than tumors with exophytic morphology. Factors as perineural infiltration, local deep structures infiltration, or regional lymph node involvement dramatically decrease survival rates.

Keywords: Pilonidal sinus. Squamous cell carcinoma. Malignant transformation.

Resumen

Objetivo: La cancerización es una complicación infrecuente pero grave de la enfermedad por sinus pilonidal. Intentaremos determinar los factores que influyen en el pronóstico de la enfermedad neoplásica basándonos en hallazgos clínicos e histopatológicos. **Material y métodos:** retrospectivamente se revisan pacientes diagnosticados de malignización de sinus pilonidal en nuestra institución del 2000 a 2019. **Resultados:** fueron recopilados los casos de siete varones con una media de edad al diagnóstico de 64.8 años. El promedio entre el inicio de los síntomas de sinus pilonidal y el diagnóstico del tumor fue de 33.7 años. Los pacientes con un patrón ulcerativo en el tumor primario presentaron todos invasión perineural, infiltración de estructuras profundas y diseminación a linfáticos regionales. Todos estos pacientes fallecieron en una media de 7 meses. Por el contrario, los pacientes que mostraban un patrón exofítico, no presentaron invasión local o afectación de los linfáticos regionales. Todos estos casos sobrevivieron, con una media de seguimiento de 70.5 meses. **Conclusiones:** tumores primarios

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ulcerativos claramente presentan un peor pronóstico que los casos de morfología exofítica. Factores como la infiltración perineural, la invasión local de estructuras profundas o la afectación de los ganglios linfáticos regionales van ligados a una disminución dramática en la supervivencia.

Palabras clave: Pilonidal sinus. Carcinoma espinocelular. Transformación neoplásica.

Introduction

Neoplastic degeneration is an uncommon but extremely severe complication of pilonidal sinus (PS). It has been estimated in about 0.01% of patients with recurrent PS, mainly in those cases which have received inadequate treatment¹. Wolff, in 1900, was the first to describe in the medical literature this infrequent condition and, to the best of our knowledge, < 100 similar cases have been reported. The most usual neoplastic degeneration is to squamous cell carcinoma (SCC), although some other reported cases presented a more infrequent evolution toward basal cell carcinoma².

In this study, we pretend to determine the factors that influence in the prognosis of the neoplastic disease assessing clinical features, histological characteristics, and evolutive profile in the patients diagnosed at our institution with malignant degeneration of PS.

Materials and methods

We conducted a review of the medical charts of patients diagnosed with PS in our department between 2000 and 2019. A specific protocol was set including comorbidities, previous records of PS disease, tumor features, oncological treatment, and follow-up. In addition, an extensive review of the current medical literature was carried out.

Results

A total of seven patients with PS malignant degeneration were diagnosed and treated at our institution during the study period (Table 1). All cases were male with a mean age at tumor diagnosis of 64.8 years old (range 46-75). Hypertension and dyslipidemia were the most common comorbidities, being present in five and three cases, respectively. All were active smokers, except one patient who was an ex-smoker.

Average time between the initial symptoms of PS disease and the tumor diagnosis was 33.7 years (range 19-43). In five cases, an antecedent of surgical drainage or an attempt of PS debridement

was recorded. In three of these cases, surgical drainage was carried out in at least two different procedures. A previous complete resection of PS was not appropriately done in any case and they all presented relapse of the disease. In three of the patients an ex-crescent, exophytic mass was described at initial tumor diagnosis; one of them also presented satellite skin lesions in a similar pattern than the primary tumor (Fig. 1). In other three patients, the lesion was described as infiltrative or ulcerative (Fig. 2). Finally, in one patient, the tumor became manifest as a persistent cutaneous swelling and occasional oozing in the past 9 months in the area affected by multiple sinus tracts (Fig. 3).

Histological studies after biopsy revealed one case of verrucous carcinoma, two cases of well-differentiated SCC and four cases of moderately-differentiated SCC. Perineural invasion in the tumor sample was demonstrated in half of the cases. Local invasion of adjacent structures as gluteal or perineal muscles, rectum or sacral bone, and neoplastic dissemination to the regional lymph nodes was assessed in three cases. Interestingly, all these cases with deep infiltration showed a tumor morphology with an ulcerative pattern and perineural invasion. Distant metastases to the lung initially appeared in only one patient (Fig. 4).

Wide surgical resection with histologically clear margins was carried out in all the patients with one exception, in which palliative chemotherapy was directly started due to Stage-IV extension, adhering to a weekly cisplatin, and 5-fluorouracil scheme, according to Al-Sarraf recommendations. In cases with affected lymph nodes, adjuvant radiation therapy was indicated after regional lymphadenectomy. In any case, the radiotherapy was delivered to the tumor bed.

In five of the six patients who underwent surgery, the coverage of the post-resection defect was carried out using regional fasciocutaneous flaps (Fig. 5). In the one remaining, it was achieved employing split-thickness skin grafts. Four patients did not present any local or regional recurrences or, distant metastases, with an average follow-up of 70.50 months (range 42-91). These four cases, neither presented

Table 1. Summary of the cases with PS malignization

Case	Age	Comorbidities	Tobacco use	Latency period (years)*	Previous procedures†	Histology	Perineural invasion	Tumor morphology	Local invasion	Pathological lymph nodes‡	Distant metastases‡	Treatment	Follow-up (months)	Disease course	Dead with disease
Case 1	56	Hypertension, dyslipidemia	Yes	28	No	Verrucous carcinoma	No	Exophytic (6.5 × 5 cm)	No (skin)	(-)	(-)	Wide surgical excision	91	No recurrence	No dead
Case 2	46	Hypertension	Yes	19	No	SCC G2	Yes	Ulcerative (8.7 × 4 cm)	Yes (rectum, perineal and gluteal muscles)	(+)	(+)	Palliative chemotherapy	13	Multiorgan progression	Yes
Case 3	60	-	Yes	43	Yes	SCC G1	Yes	Ulcerative (9 × 5 cm)	Yes (gluteal muscles, sacrum)	(+)	(-)	Wide surgical excision + lymphadenectomy + radiotherapy	6	Multiorgan progression (palliative chemotherapy)	Yes
Case 4	75	Hypertension, prostate adenocarcinoma	Yes	41	Yes	SCC G1	No	Exophytic (6 × 3.7 cm)	No (skin)	(-)	(-)	Wide surgical excision	87	No recurrence	No dead
Case 5	75	Hypertension, dyslipidemia, atrial fibrillation	No (ex-smoker)	43	Yes	SCC G2	No	Exophytic (3 × 4 cm)	No (skin, sinus tract)	(-)	(-)	Wide surgical excision + SLNB	42	No recurrence	No dead
Case 6	68	-	Yes	20	Yes	SCC G2	Yes	Ulcerative (8.5 × 7 cm)	Yes (gluteal muscle, coccyx)	(+)	(-)	Wide surgical excision + lymphadenectomy	3	Local recurrence + distant metastases (lung, dorsal vertebrae)	Yes
Case 7	75	Hypertension, dyslipidemia	Yes	42	No	SCC G2	Yes	Multifocal over sinus tracts	Yes (sacral periosteum)	(-)	(-)	Wide surgical excision + SLNB	62	No recurrence	No dead

*Duration of symptomatic pilonidal disease before the development of carcinoma.

†Previous surgical drainages or ablation of the PS.

‡At tumor diagnosis.

SCC: squamous cell carcinoma.



Figure 1. A 56-year-old male with pilonidal sinus disease for more than 28 years referred a fast grown intergluteal mass in the past 8 months. Biopsy revealed a verrucous carcinoma and complementary studies showed no affection of regional lymph nodes or distant metastases.



Figure 3. A 75-year-old male with pilonidal sinus disease for 42 years that never underwent proper surgical treatment. He presented in the past 9 months swelling, redness, and pain in a skin area affected for long-term fistulas. Surgical resection of the lesions revealed a multifocal moderately-differentiated squamous cell carcinoma over different sinus tracts. Nor regional or distant metastatic disease was assessed and 62 months after surgery no progression had been detected.



Figure 2. Male 60-year-old. At the age of 17, the patient underwent surgical drainage and debridement of an abscess in the left gluteal region and in the intergluteal fold, although no further resection was practiced. He presented at initial examination an over-scarred area in the intergluteal fold with an ulcerated lesion in the left gluteal area. Biopsy revealed a well-differentiated squamous cell carcinoma. Lymph nodes metastases were assessed in both groins. The patient passed away 6 months after surgical resection and lymphadenectomy due to multiorgan neoplastic progression.

local invasion nor regional lymph nodes involvement at the initial diagnosis, and all of them are still alive. On the other hand, the remaining three patients presented deep local invasion and regional lymph nodes affection, which developed a clinical course in a fatal way. The average time of survivance after tumor diagnosis in these latest patients was 7 months (range 3-13).

Discussion

The prevalence of PS ranges from 0.7% to 2.4%³. PS is cystic lesions in the sacrococcygeal midline which usually appear as fistulized abscesses with occasional oozing. For many years, it was debated whether PS origin was congenital, but most of the authors consider that is an acquired process⁴. Formation of the cyst in the hair follicles of the intergluteal fold can produce a foreign body reaction with a resulting infection. The neoplastic degeneration of a PS, although infrequent⁵, is the most serious complication that may occur. Indeed, these are usually described in the literature as single clinical cases and reports of three or more cases are rare. This makes it difficult not only to manage the treatment, due to a lack of scientific evidence, but also to realize a methodological diagnosis of these cases.

According to the data presented in the literature, most patients suffering from malignant degeneration of a PS are males in their fifties or older^{1,6}. However, as we describe in our second case, malignant degeneration can occur at an earlier age. The most important factor in the development of a neoplasm has been considered the latency period between the initial symptoms of the PS and the diagnosis of the tumor⁷, which, in our series, reaches three decades. In a wide-ranging review of the literature, to which they added three cases, De Bree et al. put the average latency period

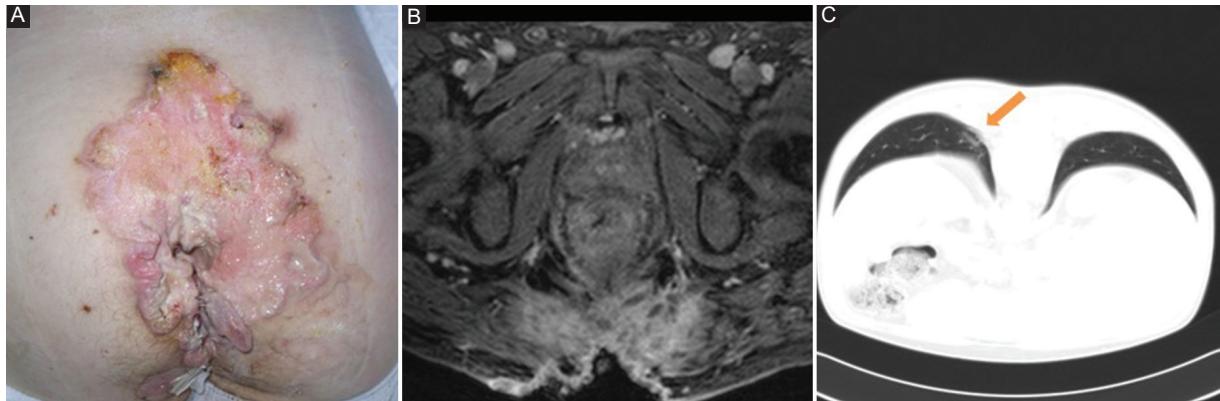


Figure 4. Male patient 46-year-old, pilonidal sinus (PS) since he was 27. **A:** he always had refused previous surgical treatment of the PS disease and consulted because ulceration and papilomatose formations in the affected area. **B:** biopsy revealed moderately-differentiated squamous cell carcinoma. Magnetic resonance imaging showed thickening of the distal third of the rectum and diffuse infiltration of the perineal and gluteal muscle. **C:** inguinal lymph nodes. Chest computed tomography revealed lung metastases. The patient died 13 months after initial tumor diagnosis despite of palliative chemotherapy.

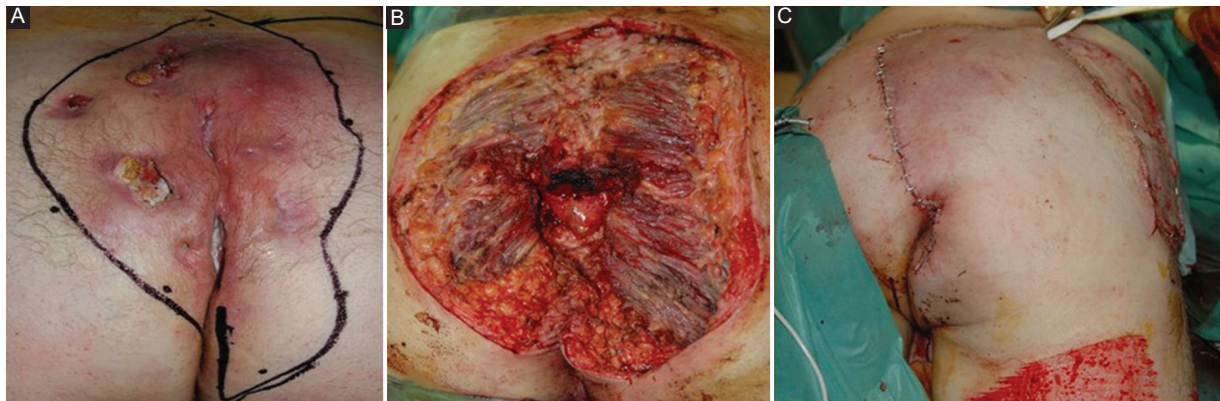


Figure 5. A: A 68-year-old male consulted with persistent bleeding through ulcerated fistulas and induration in the sacrococcygeal area in the past 9 months. Pilonidal sinus disease was diagnosed 20 years ago, and occasional abscesses were drained throughout this period. **B:** moderately differentiated squamous cell carcinoma was revealed through incisional biopsy. Computed tomography study showed bilateral affection of the inguinal lymph nodes. A complete excision of the lesion was performed including left Gluteus maximus and coccyx. **C:** intraoperative biopsy showed margins free of tumor so a transposition flap was designed to cover the defect. Three months after surgery, the patient passed away presenting local recurrence and distant metastases to lung and dorsal spin.

between the appearance of the PS and the development of a tumor at 22 years⁵.

The inflammatory process which repeatedly occurs due to infections in patients with PS has been proposed as a ethiopathogenic mechanism of malignant degeneration^{8,9}. The same factors have been suggested to explain a similar effect in other chronic inflammatory lesions or in areas of unstable scarring with repeated ulceration and healing, such as burn scars¹⁰. In the 1930s, Treves and Pack attempted to explain the ulceration and malignization of burn scars due to the effects that the toxins of the damaged tissue had on the scar itself by way of autolysis or heterolysis¹¹. Castillo, followed by Bostwick, developed hypotheses

relating malignization to the absence of a normal anatomy of the lymphatic system in the scar, this would allow the tumor to develop without the influence of the defense mechanisms of the immune system^{12,13}. The same explanation as for neoplastic degeneration of unstable burn scars can be employed here to justify malignant transformation of a chronic PS disease. Long-term active PS disease supporting this inflammatory non-healing environment could be enhanced by the negative effect of tobacco consumption. An immunohistochemical link has been demonstrated between hidradenitis suppurativa (HS) lesions and those of PSs suggesting that PS disease could be a localized form of HS¹⁴. In fact, many patients who have

HS also present PS disease. Tobacco consumption has been associated with a higher incidence of HS^{15,16} and has been raised its influence on a better prognosis of the disease when the consumption is interrupted^{17,18}. Six of our seven patients were active smokers at the time of the neoplasm diagnosis and the remaining patient was an ex-smoker.

The diagnosis of the tumor is often difficult due to the already altered anatomy because of the PS and its persistent lack of treatment. Usually, the tumor is not diagnosed until it has reached a considerable size or presents changes such as rapid ulceration or bleeding margins^{8,19}. Three of our patients were diagnosed after they developed excrescent masses in the PS affected areas; in three other cases, tumors were discovered following the development of ulceration, and finally, one tumor was diagnosed after some months of swelling and oozing through previous fistulas. This appearance of recent changes in the affected area, or the intensification of the symptoms of PS, has been widely proposed as indicating features of malignization^{5,7,20}.

A definitive diagnosis will be established by biopsies. SCC is the most frequent histological type observed; however, the development of basal-cell carcinoma and adenocarcinoma has also been described^{2,21}. SCC developed on chronic wounds, including PSs, it is known to have a worse prognosis than those grown on previously healthy skin, despite being, in most cases, moderately or well-differentiated neoplasms^{1,22,23}. According to data obtained from our own series, patients presenting tumors with an ulcerative or infiltrative pattern will have a worse prognosis than those with exophytic patterns. Moreover, we could also observe that in cases with ulcerative pattern, perineural tumor infiltration was found in the histological samples of all of them, that is well known to be a poor prognosis factor of the tumoral lesion. This fact could be of interest when we try to correlate clinical signs of suspicion of PS disease malignization before an accurate diagnosis and a poor evolution of the subjacent condition.

It should be taken into account that these tumors frequently present an extensive local infiltration, both in soft tissues (subcutaneous fat, muscle, or rectum) or in adjacent bone structures, especially in the sacrum and coccyx. A computed tomography (CT)/magnetic resonance imaging (MRI) study must be realized to know the real extension of the tumor attending to the affected deep structures due to plan the most adequate surgical treatment possible. In

addition to a physical examination, radiological exams (ultrasounds or CT if necessary) allow the regional lymph nodes to be further studied. In such cases, in which malignant degeneration of PS is concomitant with active infection, lymph node enlargement can be secondary to the infection itself. Therefore, confirmation of the real extension of the oncological process must be ensured by adequately powered studies. Fine-needle aspiration biopsy has been used as a diagnostic method in cases of palpable lymph nodes and non-palpable lymph nodes with radiological criteria of malignancy²⁴. In cases, in which lymph nodes are not palpable or imaging is not suspicious of malignancy, Sentinel Lymph Node Biopsy (SLNB) can be an efficient option to ensure step by step staging. However, indications of SLNB in high-risk cutaneous SCC are not so well established as in other tumors, such as breast cancer or melanoma²⁵. At the time of primary tumor diagnosis, we believe that a chest-abdomen-pelvis CT it is mandatory to staging all the patients with the aim of set up the most appropriate treatment scheme.

Surgical resection of the primary tumor with disease free margins is judged the best option for the initial treatment of neoplastic degeneration of PS^{5,8,22}. This includes gluteal muscles, sacrum, and coccyx if they have been affected by the tumor. In cases of rectal infiltration, it may also be necessary to perform an abdominoperineal amputation¹⁹ or even a hemipelvectomy if the pelvis floor is widely affected²⁶. In our opinion, intraoperative biopsy of the resected margins should be performed. In the case that an adequate intraoperative histopathological study could not be obtained, coverage of the defect should be delayed if possible. A delayed repair is also recommended when active infection is present²². Coverage of the post-resection defect must require in most of the cases, the use of flaps. A strict follow-up is recommended with image techniques to diagnose any local relapse occurring depth to the flap covered area.

Some authors proposed the ablation of primary tumors using cryotherapy in cases considered to be inoperable²⁷. We believe that resection of large tumors using this technique, especially if they are not only limited to the skin, cannot ensure margins of resection with the same quality for histological observation.

Radiotherapy is mainly used as an adjuvant treatment after surgery in affected lymph nodes regions. There is no consensus about its application in the primary tumor location. Some authors recommend

administration of radiation therapy after resection of the tumor in all the cases^{8,28}. Other indications depend on the tumor size, the width of the clear surgical margins or the presence of recurrence. In our series, the radiotherapy was used as an adjuvant treatment to surgery when regional nodes were affected. All these cases developed distant metastases. Radiotherapy in the primary tumor site was not administered in any case, but local relapse was only noticed in one of the cases < 3 months after surgical resection.

Despite the fact that only one of the patients included in our study presented distant metastasis at the time of diagnosis, we did observe that in cases with advanced local infiltration, metastases occurred shortly after the initial tumor diagnosis. This pattern appears to be repeated in other publications^{22,27}, in which the presence of bone or rectal infiltration, and especially, the presence of metastatic regional lymph nodes at the time of diagnosis, significantly reduce the time that the patient is free of disease and survival. Interestingly, the patient treated with chemotherapy regimen alone, had a much better surveillance than the other ones who were not, and also showed an advanced initial presentation. On the other hand, in those cases where the SCC was limited to the skin, the patients are still alive, proving the surgery to be enough for an appropriate disease control.

Conclusions

Poor treatment for extended periods of time in PS disease can lead to a carcinomatous transformation of the chronic unstable wound. The presence of ulcerated or infiltrative lesions clearly shows a more aggressive course and a worse prognosis than tumors with exophytic morphology. Factors as perineural infiltration, local deep structures infiltration, or regional lymph node involvement engage an extremely poor prognosis. Survival rates dramatically decrease when those mentioned structures are affected at the time of initial tumor diagnosis. Our study stresses the relevance of bearing in mind that PS can have a component of chronic wound, and in these instances, noteworthy changes must be always scrupulously examined to avoid a fatal outcome. Other studies to determine the role of both surgery and chemotherapy in the control of locally advanced SCC should be conducted in the future.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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