



# Ocular Metastasis in Pancreatic Cancer: Prevalence and Literature Review

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## Abstract

**Purpose:** To assess the prevalence of ocular metastasis in pancreatic cancer (PC) as little is known in the literature.

**Methods:** Prospective cross-sectional study of consecutive patients with PC at the time of initial diagnosis in one medical center. Complete eye exam was performed by a single operator. A literature review was done to collect cases of metastatic eye disease in PC.

**Results:** A total of 26 PC cases were examined at the time of cancer diagnosis before starting chemotherapy. The mean age was 66.4 years with 22 men and 4 women. Seventeen patients (65.4%) had metastatic disease at presentation. Metastasis to the ocular region was not detected clinically. Literature review of 35 cases of PC with metastatic eye disease revealed choroidal (18 cases-51.4%), orbital (6 cases-17.1%) and extraocular muscle (5 cases-14.3%) involvement.

**Conclusion:** PC is a rare cause of metastasis to the uvea or orbit.

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**Keywords:** Metastasis; Orbital metastasis; Pancreatic cancer; Uveal metastasis.

## Introduction

Pancreatic Cancer (PC) has a very poor prognosis with very low survival rate. Risk factors include alcohol consumption, smoking, and familial history [1]. Few retrospective reports of metastasis from pancreatic cancer to the ocular region have been reported in the literature [2-27]. **(Table 1)** [2-34] the aim of this study is to assess the prevalence of ocular metastasis in patients with newly diagnosed PC prior to medical treatment.

## Methods

This is an institutional Review Board approved (SUR.WF.04) prospective study of newly diagnosed PC cases presenting to the American University of Beirut Medical Center from February 2016 to February 2020. Inclusion criteria included ability to understand and sign a written consent form, and age above 18 years. Exclusion criteria included the presence of a second primary cancer besides PC, and previous treatment with chemotherapy, radiotherapy, brachytherapy, or surgery.



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All patients underwent eye examination including spectacle-corrected visual acuity, tonometry, slit-lamp biomicroscopy, and a dilated fundus examination by a senior examiner (AMM).

Literature review was done using the search terms of 'ocular metastases' AND 'PC'. The databases of Medline, Embase and Google Scholar were systematically searched for relevant articles published between 1975 and May 2020. Forward searching, checking references in major reviews on PC and in all retrieved articles were also done.

## Results

A total of 26 patients (52 eyes) had an ophthalmologic evaluation. Of the 26, there were 22 men and 4 women. The mean  $\pm$  standard deviation age was  $66.4 \pm 11.1$  (range 40-86). The mean body mass index was  $26.1 \pm 5.3$  (range 15-36.8). Systemic diseases included diabetes mellitus (10), systemic hypertension (11), and coronary artery disease (3). Fifteen patients were smokers and 10 patients were alcoholic. The histopathology was ductal adenocarcinoma. Staging according to the American Joint Committee on Cancer Staging was as follows: IA (1), IB (2), IIA (6), IIB (2), III (2), IV (7) and no classification made at time of eye exam (6). Nine patients had no sign of systemic metastases at the time of the eye exam. Metastases were detected in 17 patients as follows: 12 had liver metastases, 8 had abdominal wall metastases, 2 had lung metastasis, 2 had bone metastasis, and 7 had positive lymph node metastases. Four patients had a family history of malignancy.

All patients had no evidence of metastatic eye disease. One patient developed venous stasis retinopathy in one eye on follow-up and also another patient developed bilateral reversible visual loss from maculopathy secondary to mitogen-activated protein kinase enzymes inhibitor.

The systematic review of the literature (Table 1) yielded 35 cases of metastatic PC to the ocular region. The three commonest sites involved included: choroidal disease (18 cases or 51.4%), orbital disease (6 cases or 17.1%) and extraocular muscle disease (5 cases or 14.3%). Besides direct invasion, other remote effects included cancer associated retinopathy, paraneoplastic optic neuropathy, paraneoplastic opsoclonus myoclonus and Purtscher-like retinopathy.

## Discussion

In our study, all patients were negative for any ocular metastasis. It is possible that the low metastatic rate relates to the eye exam being performed early in the disease at the time of diagnosis (and not later when metastases may be more widespread), and also to the short life span of patients. One hallmark of PC is fast local progression and early systemic dissemination at various sites. This unique process of PC initiation, progression and metastasis explains the propensity of PC to spread to the liver, abdominal wall, lung and bone yet spares the ocular region for yet unknown reasons. Shah et al [28] reported 5 patients out of 1123 with metastasis to the choroid detected after the diagnosis of PC by a mean interval of 34 months (range 12-60 months). In a review of 302 patients dying of cancer, 12 had PC and no ocular metastases were detected histologically at the Wisconsin Eye Bank [18]. In a larger series of 741 patients dying of cancer at the Wilmer Eye Institute, 28 patients had PC and only one patient had ocular metastasis late in the disease [18].

In the current review of the literature of metastatic PC, around half of the cases involved the uveal tract and the rest

the extraocular muscles (recti) or orbit or the optic nerve. Choroidal metastases from PC, like in most other carcinomas, were yellow in color, have a plateau configuration, and are commonly associated with subretinal fluid [4]. Rarely the mass can mimic a choroidal melanoma with a mushroom appearance on ultrasound [5]. They are most commonly solitary and unilateral [28] with few cases being multiple or bilateral [17]. The detection of the choroidal mass usually occurred sometime following metastasis to the liver or bone or elsewhere [17].

Similarly, orbital or extraocular muscle metastases from PC manifested as diplopia, proptosis or ptosis like other malignancies [19]. The most known neoplasms that metastasize to the orbit originate from breast carcinoma, lung carcinoma, prostatic carcinoma, and melanoma [19,35]. It is well known that metastases to extraocular muscles are very rare, accounting for less than 10% of all orbital metastases [35]. It is our impression that there may be a preferential metastasis to the extraocular muscles in PC, but this could also relate to a literature bias.

The current cross-sectional study suffers from a small number of patients, lack of a follow-up. In conclusion, pancreatic cancer rarely metastasizes to the ocular region.

**Table 1:** Literature review of pancreatic cancer metastatic to the eye and orbit: 35 cases [2-27].

<b>Choroid 18 cases: 8 cases [2], 2 cases [4], 1 case [3,5,6,7,9,16,17]</b>
<b>Orbit 6 cases [15,20,21,23,24,27]</b>
<b>Extraocular muscle 5 cases: 2 cases [13], 1 case [15,19,25]</b>
<b>Iris 1 case [8]</b>
<b>Optic nerve 1 case [14]</b>
<b>Orbital apex 1 case [26] Third nerve palsy</b>
<b>Metastatic disease with site not specified 3 cases (2 cases [18], 1 case [22])</b>
<b>Others</b>
Cancer associated retinopathy 1 case [29]
Paraneoplastic optic neuropathy 4 cases [30]
Paraneoplastic opsoclonus myoclonus 3 cases [31,32]
Purtscher-like retinopathy

## Statement of ethics

The study was performed ethically in accordance with the World Medical Association Declaration of Helsinki. The subjects gave their informed consent to be examined and report the results of their exam and the study protocol was approved by the institute's clinical research office.

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**Author contributions:** HAM, WF, AMM wrote the text. MJK, MK, AS, DM contributed data and edited the text.

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