

CASE REPORT

PEER REVIEWED | OPEN ACCESS

# An advanced case of breast implant-associated anaplastic large cell lymphoma

C Cullinane, P O Leary, M J O'Sullivan, M A Corrigan, N Marshall, T J Browne, J Kelly, H P Redmond, L Kelly

## ABSTRACT

**Introduction:** Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare type of non-Hodgkin lymphoma that was first described in the literature in 1997. The most common clinical presentation of BIA-ALCL is a persistent seroma, which can be accompanied by breast swelling, asymmetry, or pain. Approximately 30% of patients present with a tumor mass. **Case Report:** A 66-year-old woman underwent bilateral mastectomies and immediate implant reconstruction for screen detected ductal carcinoma in situ (DCIS) of the right breast in January 2016. Four years later the patient presented with a right breast mass that developed over a period of weeks. Radiological and pathological investigations confirmed the presence of multifocal mass forming BIA-ALCL with axillary, sub-pectoral, and intra-mammary lymph node involvement. Following multi-disciplinary team (MDT) input, definite was surgery and was also performed. En bloc resection of the right breast tumors and capsulectomy was performed in parallel with left breast explantation and capsulectomy. An axillary lymph node clearance of the right axilla was performed. The patient had an uneventful postoperative recovery and was discharged on post-operative day 5. Following MDT discussion the patient is awaiting adjuvant chemo/radiation therapy. **Conclusion:** All patients

presenting with a delayed spontaneous seroma (>1 year after implantation) after placement of a textured implant should be investigated for BIA-ALCL. In the majority of cases explantation and total capsulectomy is curative and patients will have an excellent survival outcome.

**Keywords:** Anaplastic, Breast implant, Lymphoma

### How to cite this article

Cullinane C, Leary PO, O'Sullivan MJ, Corrigan MA, Marshall N, Browne TJ, Kelly J, Redmond HP, Kelly L. An advanced case of breast implant-associated anaplastic large cell lymphoma. Int J Case Rep Images 2020;11:101148Z01CC2020.

Article ID: 101148Z01CC2020

\*\*\*\*\*

doi: 10.5348/101148Z01CC2020CR

## INTRODUCTION

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare type of non-Hodgkin lymphoma that was first described in the literature in 1997 [1]. The first case of BIA-ALCL described a 41-year-old woman with a CD30+ peripheral T-cell lymphoma mass surrounding a cosmetic textured-surface breast implant [1]. Since 1997 more than 500 cases of breast implant-associated anaplastic large cell lymphoma have been reported across 29 countries worldwide [2]. Breast implant-associated anaplastic large cell lymphoma was provisionally classified in the 2016 revision of the World Health Organization classification of lymphoid neoplasms [3]. In 2019, the U.S. Food and Drug Administration released a statement reporting the lifetime risk for breast implant ALCL is between 1 in 3817 and 1 in 30,000 women with textured breast implants [4]. The median

C Cullinane<sup>1</sup>, P O Leary<sup>1</sup>, M J O'Sullivan<sup>1</sup>, M A Corrigan<sup>1</sup>, N Marshall<sup>2</sup>, T J Browne<sup>3</sup>, J Kelly<sup>4</sup>, H P Redmond<sup>1</sup>, L Kelly<sup>1</sup>

**Affiliations:** <sup>1</sup>Department of Breast Surgery, Cork University Hospital, Cork, Ireland; <sup>2</sup>Department of Radiology, Cork University Hospital, Cork, Ireland; <sup>3</sup>Department of Pathology, Cork University Hospital, Cork, Ireland; <sup>4</sup>Department of Plastic Surgery, Cork University Hospital, Cork, Ireland.

**Corresponding Author:** C Cullinane, Department of Breast Surgery, Cork University Hospital, Cork, Ireland; Email: carolyncullinane@rcsi.com

Received: 11 June 2020  
Accepted: 06 July 2020  
Published: 28 July 2020

interval from time of implant insertion to diagnosis of BIA-ALCL is between 7 and 10 years [5, 6]. The most common clinical presentation of BIA-ALCL is a persistent seroma, which can be accompanied by breast swelling, asymmetry, or pain [5]. Axillary lymphadenopathy has been reported in up to 15% of cases and approximately 20% of patients present with a mass around the implant [5, 7]. Small subsets of patients with BIA-ALCL present with cutaneous symptoms such as a skin rash or pruritis and others are diagnosed incidentally at the time of implant exchange or removal [8]. Given the novel and rare nature of BIA-ALCL clinical decision-making relies on retrospective series, case reports, and expert opinions. We present an interesting case of advanced BIA-ALCL in a 66-year-old woman.

## CASE REPORT

A 66-year-old woman underwent bilateral mastectomies and immediate implant reconstruction for screen detected ductal carcinoma in situ (DCIS) of the right breast in January 2016. The patient requested to have a contralateral left breast risk-reducing mastectomy and immediate implant based reconstruction at the time of her surgery. The patient was counseled on the additional risks and null survival benefit of contralateral surgery prior to surgery. Following surgery the patient made an excellent recovery and was prescribed adjuvant hormonal manipulation in the form of an aromatase inhibitor.

The patient had expressed some discontent over the position of the left reconstructed breast as she felt the implant migrated laterally and attended a consultant plastic surgeon in January 2020. At this time clinical examination was normal. In April 2020, the patient presented to the emergency department with a red right breast and palpable mass at the lateral edge of the implant. No effusion/seroma was appreciated. She was systemically well with mildly elevated inflammatory markers. An ultrasound was performed which revealed an ill-defined mass in the lateral right breast with associated axillary and internal mammary lymphadenopathy. A core biopsy was obtained which reported chronic inflammatory cells of indeterminate significance. Fine needle aspirate of the axillary node showed atypical lymphoid cells positive for CD30. Findings were reported as highly suggestive for a T-cell lymphoma. Magnetic resonance imaging confirmed the presence of a 45 × 37 × 28 mm mass involving the posterior capsule onto the right lateral chest wall (Figure 1). A further second mass measuring 20 mm was found in the anterior chest wall extending into the intercostal space. Internal mammary, axillary, and sub-pectoral lymph nodes were also reported. A computed tomography (CT) of the thorax, abdomen and pelvis, and positron emission tomography-computed tomography (PET-CT) scan did not reveal any visceral metastases. Due to diagnostic uncertainty at this

stage, the patient proceeded to right explantation and excision biopsy of the fixed tumor mass.

Histological analysis of the excision biopsy of the right lateral chest wall confirmed the presence of breast implant-associated anaplastic T-cell lymphoma. Following discussions at various multi-disciplinary team (MDT) meetings, the patient proceeded to have an en bloc resection of right chest wall mass with complete capsulectomy and axillary lymph node clearance. Left explantation and capsulectomy were performed simultaneously. Cardiothoracic surgery and plastic surgery were involved in the surgical decision-making process and their expertise made available if required. Sub-pectoral and axillary lymph nodes were removed; internal mammary nodes were left in situ as a marker of chemotherapy/radiotherapy response as per MDT discussion. The right lateral tumor mass and anterior chest wall mass were resected en bloc with right capsulectomy. The aim was to achieve clear margins (R0 resection) without compromising pleural integrity. The anterior chest wall mass was adherent to the anterior ribs, however a plain of dissection was adequately achieved (Figures 2–7). The histopathology report of the right breast capsulectomy revealed multifocal nodular involvement of large markedly atypical lymphoid cells with the largest nodule measuring 10 × 3.5 cm. Skeletal muscle was focally involved at the deep margin and this was deemed non improvable surgically. Two out of seven axillary lymph nodes showed involvement and partial nodal sinusoidal involvement by BIA-ALCL. Immunohistochemical studies showed atypical lymphoid cells showing partial positivity with cutaneous lymphocyte-associated antigen (CLA) with the majority of cells being positive with the T-cell markers CD43, CD4, and MUM1. The tumor was strongly diffusely CD30 positive and ALK1 negative. The patient made an excellent post-operative recovery and was discharged on post-operative day 5. Following MDT discussion the patient will receive adjuvant chemotherapy (CHOP regime) and radiotherapy with the aim of reducing the risk of loco-regional or systemic recurrence. Clinical review will be on a three monthly basis.

Three weeks after the patient was diagnosed, a second patient was diagnosed with BIA-ALCL in the same department. This patient presented more typically with a seroma and cytological analysis revealed atypical lymphoid cells positive for CD30 and negative for ALK 1. Curative surgery in the form of a left capsulectomy was performed with no further treatment required.

Both cases illustrate the complex nature of the disease and how the clinical presentation can vary.

## DISCUSSION

To the best of our knowledge this is the first documented case of BIA-ALCL in the Republic of Ireland. The primary risk factor for developing BIA-ALCL is exposure to textured implants. To date, there are no

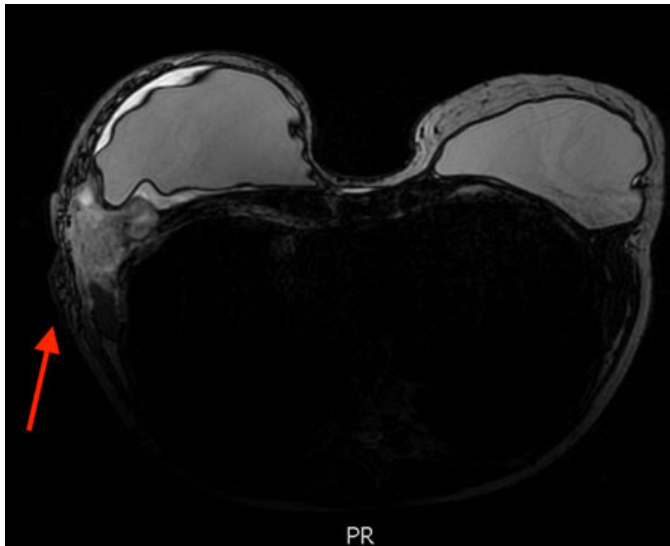


Figure 1: T2-weighted MRI image of bilateral reconstructed breast. Red arrow points to right chest wall lymphoma mass.



Figure 2: Pre-operative image on the operating table of right reconstructed breast with right lateral tumor mass.

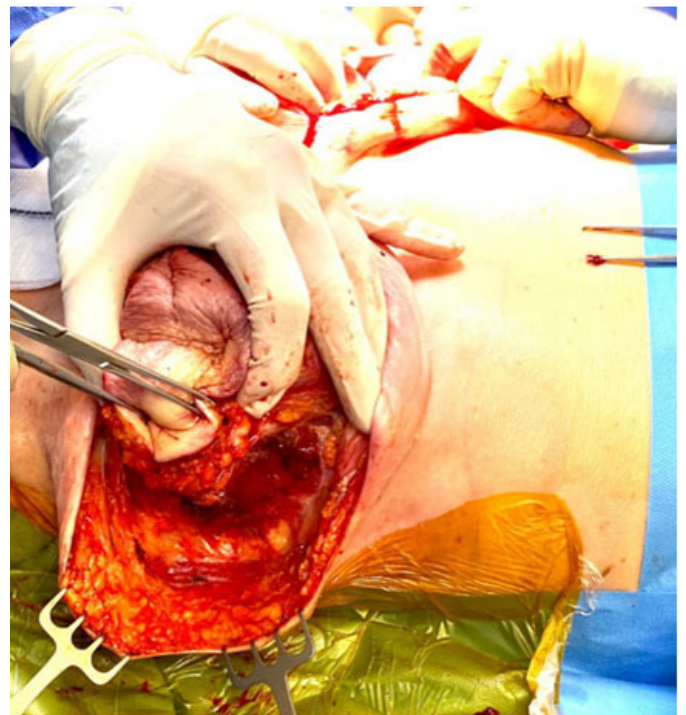


Figure 3: Right breast lateral tumor mass resected en bloc with right capsule.

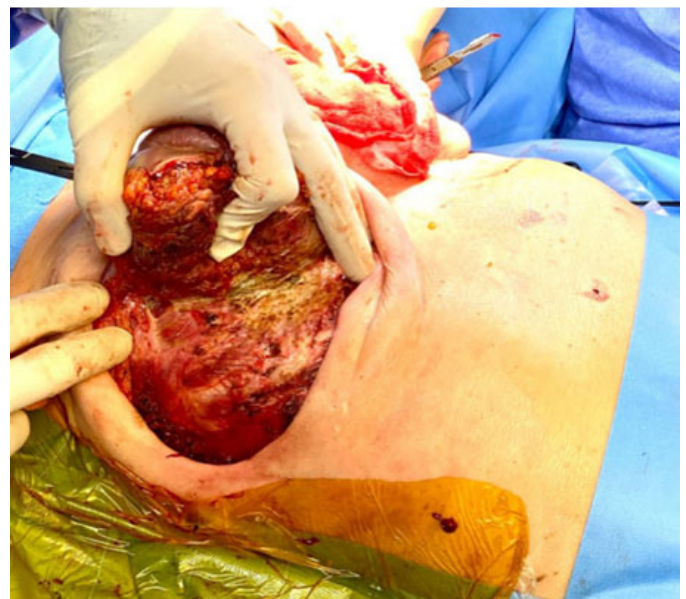


Figure 4: Intra-operative image of dissection plain between tumor and chest wall.

reported cases in patients with smooth implants only [5, 7, 9]. The precise pathogenesis of BIA-ALCL is unclear with multiple hypotheses proposed. One such theory hypothesizes that the hosts' T-cell (cytotoxic and helper) response to the particulate on the textured implant surface is a potential pathological driving force [10, 11]. Textured implants are different to smooth implants because they shed particulate matter. Macrophages auto digest this particulate to form foamy cells and secrete pro-inflammatory cytokines such as interleukin-1, interleukin-6, and tumor necrosis factor which in turn leads to T-cell chemotaxis and replication [12, 13]. An alternative theory of pathogenesis involves colonization of gram-negative bacteria in a biofilm surrounding

the implant producing lymphocyte hyperplasia [14]. Both theories infer that the underlying pathological mechanism of BIA-ALCL is a result of aberrant reactive T-cell lymphoproliferation. From a cancer genomics perspective, activating somatic mutations in the JAK-STAT signaling pathway, SOCS1, TP53, and DNMT3A have been described in BIA-ALCL [15, 16]. Intriguingly germ line mutations in the JAK3 signaling pathway

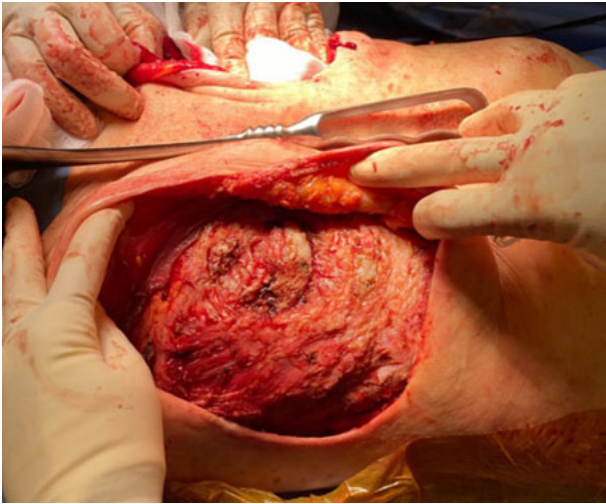


Figure 5: Intra-operative image post en bloc resection of right breast tumor masses and capsule. Ribs visible.

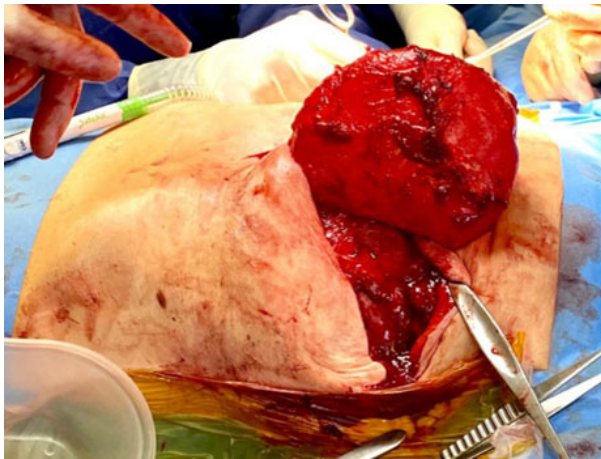


Figure 6: Intra-operative image of left capsulectomy. Implant and capsule excised as single specimen intact.



Figure 7: Right breast en bloc resection specimen sent for histopathological assessment.

have been identified in some patients with BIA-ALCL suggesting certain innate host factors may predispose to the development of BIA-ALCL [17]. Considering the novel nature of this disease, the pathogenesis and genetic drivers underlying BIA-ALCL are still unclear and further research is needed in this area.

BIA-ALCL has been described in women who have undergone breast implantation for cosmetic and reconstructive options. The most common clinical presentation is delayed seroma (>1 year after implantation) surrounding the implant, this occurs in two-thirds of patients [5]. The term seroma is incorrect in the context of this disease as a seroma by definition contains transudative fluid with a low protein count. The fluid surrounding the implant in BIA-ALCL contains liquefied and necrotic lymphoma cells with a high protein content, therefore the term effusion should be more accurately adopted [18]. Our case was unusual in that she presented with a tumor mass and skin changes overlying the reconstructed breast. No appreciable effusion was detected. Approximately 30% of patients present with a tumor mass which is usually palpable along the medial or lateral surface of the implant. In the case of our patient, the fixed tumor mass was palpable over the lateral border of the implant and increased in size over a period of weeks.

The National Comprehensive Cancer Network (NCCN) has outlined the diagnostic work-up required for BIA-ALCL [19]. Any effusion occurring greater than one year after implantation that is not readily explained by infection or trauma should be suspected for BIA-ALCL. Ultrasound guided aspiration of periprosthetic seroma fluid for microbiological analysis and cytology assessment is required. Magnetic resonance imaging of the breasts is required for assessment of implants integrity and tumor mass. In the case of mass forming BIA-ALCL, cytological aspirate assessment should be geared toward adenocarcinoma as well as lymphoma diagnoses [19]. Immunohistochemistry should be performed to determine the immunophenotype. CD30 is expressed in all cases of BIA-ALCL and ALK 1 is typically negative. CD30 is characteristic of BIA-ALCL but not specific as it also expressed in various other lymphoid malignancies [20]. If a tumor mass is detected pre-operatively, en bloc resection with clear margins is recommended. Patients presenting with an effusion require explantation and complete capsulectomy and this is curative for many patients [8, 19].

Breast implant-associated anaplastic large cell lymphoma is commonly regarded as having an indolent clinical course, and the majority of patients achieve complete remission with surgery alone [21]. A study conducted by Miranda et al. [22] reporting the long-term follow-up of 60 BIA-ALCL patients concluded that most patients achieve complete remission (72% and 93% for patients presenting with and without a mass, respectively). Advanced BIA-ALCL describes patients with bilateral breast disease, lymph node involvement, and visceral

metastasis. Complete remission rate for patients with lymph node involvement was 67% in a study conducted by Collins et al. in 2019 [21]. This cohort of patients require definitive surgery (explantation, capsulectomy, and tumor resection), chemotherapy, and radiotherapy to optimize survival outcomes [21]. The trajectory toward a poorer outcome for patients with advanced disease was attributed to a delay in diagnosis and definite surgery. Our case was diagnosed and underwent definite surgery within four weeks which will hopefully translate into a good outcome for the patient.

## CONCLUSION

Breast implant-associated anaplastic large cell lymphoma is a rare condition that is gaining recognition and awareness due to continued research and publications in the area. All patients presenting with a delayed spontaneous seroma (>1 year after implantation) after placement of a textured implant should be investigated for BIA-ALCL. Seroma fluid should be aspirated and screened for lymphoma using CD30 immunohistochemistry and flow cytometry. In the majority of cases explantation and total capsulectomy is curative and patients have an excellent survival outcome.

## REFERENCES

1. Keech JA Jr, Creech BJ. Anaplastic T-cell lymphoma in proximity to a saline-filled breast implant. *Plast Reconstr Surg* 1997;100(2):554-5.
2. Doran EL, Miranda RN, Selber JC, et al. U.S. Epidemiology of breast implant-associated anaplastic large cell lymphoma. *Plast Reconstr Surg* 2017;139(5):1042-50.
3. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood* 2016;127(20):2375-90.
4. The United States Food and Drug Administration. Breast Implant Associated-Anaplastic Large Cell Lymphoma (BIA-ALCL) - Letter to Health Care Providers. 2019. [Available at: <https://www.fda.gov/medical-devices/letters-health-care-providers/breast-implant-associated-anaplastic-large-cell-lymphoma-bia-alcl-letter-health-care-providers>]
5. Clemens MW, Medeiros LJ, Butler CE, et al. Complete surgical excision is essential for the management of patients with breast implant-associated anaplastic large-cell lymphoma. *J Clin Oncol* 2016;34(2):160-8.
6. Leberfinger AN, Behar BJ, Williams NC, et al. Breast implant-associated anaplastic large cell lymphoma: A systematic review. *JAMA Surg* 2017;152(12):1161-8.
7. Loch-Wilkinson A, Beath KJ, Knight RJW, et al. Breast implant-associated anaplastic large cell lymphoma in Australia and New Zealand: High-surface-area textured implants are associated with increased risk. *Plast Reconstr Surg* 2017;140(4):645-54.
8. Quesada AE, Medeiros LJ, Clemens MW, Ferrufino-Schmidt MC, Pina-Oviedo S, Miranda RN. Breast implant-associated anaplastic large cell lymphoma: A review. *Mod Pathol* 2019;32(2):166-88.
9. Brody GS, Deapen D, Taylor CR, et al. Anaplastic large cell lymphoma occurring in women with breast implants: Analysis of 173 cases. *Plast Reconstr Surg* 2015;135(3):695-705.
10. Barr SP, Hill EW, Bayat A. Novel proteomic assay of breast implants reveals proteins with significant binding differences: Implications for surface coating and biocompatibility. *Aesthet Surg J* 2018;38(9):962-9.
11. Brown T, Harvie F, Stewart S. A different perspective on breast implant surface texturization and anaplastic large cell lymphoma (ALCL). *Aesthet Surg J* 2019;39(1):56-63.
12. Lechner MG, Megiel C, Church CH, et al. Survival signals and targets for therapy in breast implant-associated ALK-anaplastic large cell lymphoma. *Clin Cancer Res* 2012;18(17):4549-59.
13. Wolfram D, Rabensteiner E, Grundtman C, et al. T regulatory cells and TH17 cells in peri-silicone implant capsular fibrosis. *Plast Reconstr Surg* 2012;129(2):327e-37.
14. Hu H, Johani K, Almatroudi A, et al. Bacterial biofilm infection detected in breast implant-associated anaplastic large-cell lymphoma. *Plast Reconstr Surg* 2016;137(6):1659-69.
15. Blombery P, Thompson ER, Jones K, et al. Whole exome sequencing reveals activating JAK1 and STAT3 mutations in breast implant-associated anaplastic large cell lymphoma. *Haematologica* 2016;101(9):e387-90.
16. Di Napoli A, Jain P, Duranti E, et al. Targeted next generation sequencing of breast implant-associated anaplastic large cell lymphoma reveals mutations in JAK/STAT signalling pathway genes, TP53 and DNMT3A. *Br J Haematol* 2018;180(5):741-4.
17. Mehta-Shah N, Clemens MW, Horwitz SM. How I treat breast implant-associated anaplastic large cell lymphoma. *Blood* 2018;132(18):1889-98.
18. Miranda RN, Aladily TN, Prince HM, et al. Breast implant-associated anaplastic large-cell lymphoma: Long-term follow-up of 60 patients. *J Clin Oncol* 2014;32(2):114-20.
19. Clemens MW, Horwitz SM. NCCN consensus guidelines for the diagnosis and management of breast implant-associated anaplastic large cell lymphoma. *Aesthet Surg J* 2017;37(3):285-9.
20. Taylor CR, Siddiqi IN, Brody GS. Anaplastic large cell lymphoma occurring in association with breast implants: Review of pathologic and immunohistochemical features in 103 cases. *Appl Immunohistochem Mol Morphol* 2013;21(1):13-20.
21. Collins MS, Miranda RN, Medeiros LJ, et al. Characteristics and treatment of advanced breast implant-associated anaplastic large cell lymphoma. *Plast Reconstr Surg* 2019;143(3S):41S-50.
22. Miranda RN, Aladily TN, Prince HM, et al. Breast implant-associated anaplastic large-cell lymphoma: Long-term follow-up of 60 patients. *J Clin Oncol* 2014;32(2):114-20.

\*\*\*\*\*

## Acknowledgements

We would like to acknowledge Dr. Peter G Cordeiro from Memorial Sloan Kettering for his expert opinion contribution to the management of this case.

## Author Contributions

C Cullinane – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

P O Leary – Conception of the work, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

M J O'Sullivan – Design of the work, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

M A Corrigan – Design of the work, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

N Marshall – Design of the work, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

T J Browne – Design of the work, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

J Kelly – Design of the work, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

H P Redmond – Design of the work, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

L Kelly – Conception of the work, Design of the work, Acquisition of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

## Guarantor of Submission

The corresponding author is the guarantor of submission.

## Source of Support

None.

## Consent Statement

Written informed consent was obtained from the patient for publication of this article.

## Conflict of Interest

Authors declare no conflict of interest.

## Data Availability

All relevant data are within the paper and its Supporting Information files.

## Copyright

© 2020 C Cullinane et al. This article is distributed under the terms of Creative Commons Attribution License which permits unrestricted use, distribution and reproduction in any medium provided the original author(s) and original publisher are properly credited. Please see the copyright policy on the journal website for more information.

Access full text article on  
other devices



Access PDF of article on  
other devices





INTERNATIONAL JOURNAL OF  
CASE REPORTS AND IMAGES



VIDEO JOURNAL OF  
CLINICAL RESEARCH



VIDEO JOURNAL OF  
BIOMEDICAL SCIENCE



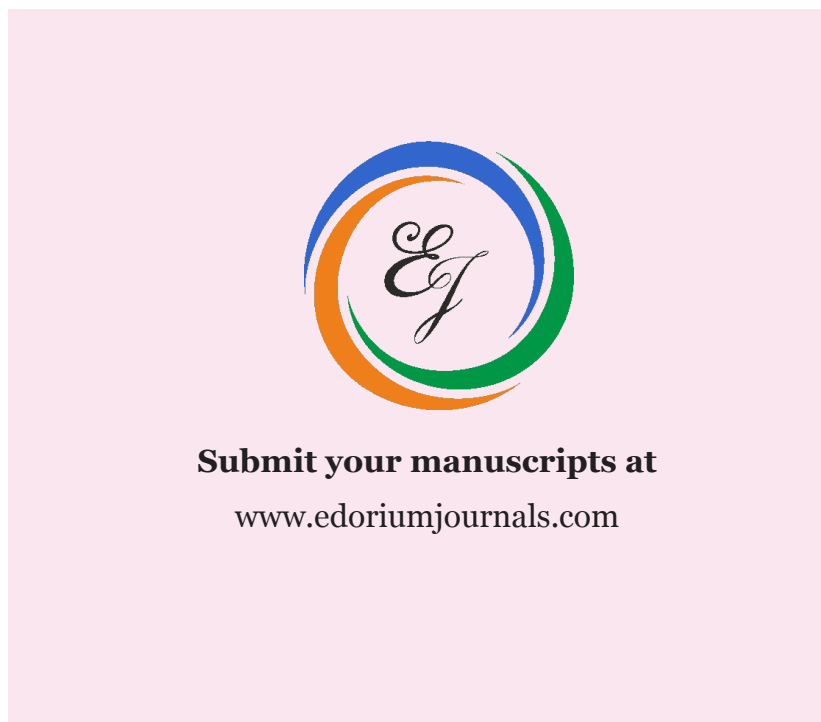
INTERNATIONAL JOURNAL OF  
HEPATOBIILIARY AND  
PANCREATIC DISEASES



INTERNATIONAL JOURNAL OF  
BLOOD TRANSFUSION AND  
IMMUNOHEMATOLOGY



EDORIUM JOURNAL OF  
OPHTHALMOLOGY



EDORIUM JOURNAL OF  
MEDICINE



EDORIUM JOURNAL OF  
CARDIOTHORACIC AND  
VASCULAR SURGERY



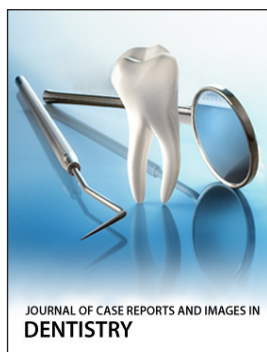
JOURNAL OF CASE REPORTS  
AND IMAGES IN ORTHOPEDICS  
AND RHEUMATOLOGY



EDORIUM JOURNAL OF  
PSYCHOLOGY



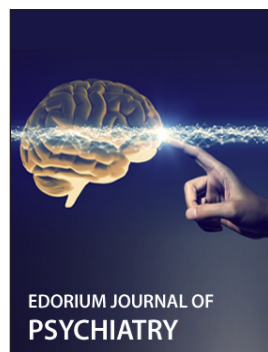
EDORIUM JOURNAL OF  
CELL BIOLOGY



JOURNAL OF CASE REPORTS AND IMAGES IN  
DENTISTRY



EDORIUM JOURNAL OF  
CANCER



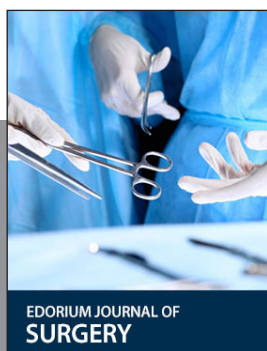
EDORIUM JOURNAL OF  
PSYCHIATRY



JOURNAL OF CASE REPORTS AND  
IMAGES IN INFECTIOUS DISEASES



EDORIUM JOURNAL OF  
ANATOMY AND EMBRYOLOGY



EDORIUM JOURNAL OF  
SURGERY



JOURNAL OF CASE REPORTS  
AND IMAGES IN PATHOLOGY



EDORIUM JOURNAL OF  
ANESTHESIA