

Histological and clinical analysis of knee cyclops lesions

Giuseppe Aloisi¹, Remo Goderecci², Andrea Fidanza¹, Gianluca Cipolloni³, Vittorio Calvisi¹

¹Department of Life Health & Environmental Sciences, University of L'Aquila, Unit of Orthopaedics and Traumatology, Coppito (AQ), Italy; ²Unit of Orthopaedics and Traumatology, Civil Hospital of Teramo, ASL 4 Teramo, Teramo, Italy; ³Department of Anatomic Pathology and Histology, San Camillo De' Lellis Hospital, Rieti, Italy

Abstract. *Background and aim:* Cyclops Syndrome, first described by Jackson and Schaefer in 1990, is known as a complication of anterior cruciate ligament reconstruction (ACLR). However further researches have demonstrated that cyclops can be present even without symptoms and/or in absence of ACLR, simply configuring itself as a lesion in patients with rupture of the native ligament. *Methods:* This is a retrospective cohort study in which we report our experience of 13 cyclops lesions found between 126 patients during a primary arthroscopic ACLR. Preoperative examination with tests of joint stability and range of movement measurement was performed and recorded. Accurate joint examination was performed during arthroscopy and the cyclops lesions found were removed and analyzed with haematoxylin-eosin coloration. Post-operative clinical examination was performed until 6 months of follow-up. *Results:* Histological analysis showed proliferation of dense fibroelastic polypoid nodules with a macroscopically histological aspects of a "blue eye", hence the name Cyclops. At 6 months of follow-up after surgery, none of the patients reported pain at terminal extension or instability and they were all able to resume their previous activities. *Conclusions:* Our study confirmed that surgical reconstruction of the ACL is not the only condition in which the Cyclops Syndrome develops; in fact our histological analysis indicate that the Cyclops lesions develop like a reactive fibroproliferative process following the rupture of the native ACL fibers, as scar reaction to the trauma: for this reason an accurate arthroscopic detection of these Cyclops lesions is crucial during primary ACL reconstruction in order to obtain the best surgical outcomes. (www.actabiomedica.it)

Key words: Cyclops syndrome, Cyclops lesions, ACL reconstruction, Knee Arthroscopy, Histological analysis

Introduction

Cyclops Syndrome is known as a complication of anterior cruciate ligament reconstruction (ACLR) and it is an important cause of reoperation after ACLR.

It was first described by Jackson and Schaefer (1) in 1990. It has been defined as a loss of knee extension due to impingement of a pedunculated proliferative tissue mass after anterior cruciate ligament reconstruction. The nodule was named in this way due to its arthroscopic appearance resembling an eye. They thought bone and cartilage residues remaining in the joint after tunnel drilling caused it. Later different

authors proposed various other causes and a multifactorial cause were suggested (2-10).

Only recently, thanks to different studies (11-16) it has been discovered that the cyclops can be present, even without symptoms, in patients with rupture of the native ligament even in absence of reconstruction, simply configuring it as cyclopean or cyclopean-like lesions.

Since all the cited studies report a limited number of cases, the purpose of this study is to add our case series in order to confirm the hypothesis that cyclops injuries can be found both in patients with a new ACL graft rupture, and in patients with a rupture of the native ACL.

Patients and methods

This is a retrospective cohort study on 126 patients that were operated at our institution for ACL rupture between January 2018 and July 2019.

All patients of both sex, between 18 and 60 years, with a clinical diagnosis of ACL primitive rupture eligible for ligament reconstruction, with or without concomitant meniscal and/or collateral ligament lesions met the inclusion criteria (17).

Exclusion criteria were: patients non eligible for surgery and history of rheumatic diseases.

The study group consists of 11 males and 2 females with an average age of 32.4 years (24-54).

The patients referred a damaging event that occurred as a result of a change of direction, slippage or contact trauma, especially during a sport practice.

In objective pre-operative examination all patients referred pain, swelling and joint instability. Preoperative stress-tests were performed in order to identify the joint instability due to ACL lesion: anterior Drawer test, Posterior Drawer, Lachman and Jerk, valgus and varus stress tests; the presence or absence of joint noises (clunk) were recorded.

All patients with an ACL rupture were surgically treated using the same procedure protocol: first of all, a diagnostic arthroscopy using anterolateral, anteromedial and a modified midpatellar portal (mMPP) (18) was performed to confirm the ACL lesion and, where present, nodules adhering to the anterolateral part of the ACL near tibial insertion were identified, all removed and the samples collected for biopsy; if found, other joint injuries were treated (for example meniscectomy, meniscal suture, cartilage lesion debride or reconstruction etc.)(19,20); finally, the semitendinosus and gracile tendons were both harvested, triplicated and doubled, to obtain a graft of at least 8 mm of diameter. All ACLR were performed through the transtibial technique and the grafts were fixed proximally by Rigidfix and distally with a Milagro Screw.

All patients followed the same rehabilitation protocol following the arthroscopic reconstruction: knee brace locked in extension for seven days, later unlocked joint at 90°, walking with crutches with progressive weight bearing for twenty-one days, progressive muscle strengthening exercises and cryotherapy.

The collected nodules have been placed in suitable containers with 10% buffered formalin and sent to pathology laboratory for the histological analysis.

Once the fixing phase was completed, the samples were processed with graduated concentrations of alcohols and xylene. The histological cassettes, taken from the automatic processor, were placed in the hot room of the inclusion unit, opened and filled with liquid paraffins (temperature 56°-57°). Subsequently, microtome cuts of 3-4 microns of thickness were realized, collected on slides and colored. The coloring used for all samples was the haematoxylin-eosin. Haematoxylin is extracted from the bark of a tropical tree (haematoxylon campechianum), it's characterized by positive charge and it typically colors the nucleus by binding with metal salts. Eosin is an anionic dye that electrostatically combines with different cytoplasmic components and several extracellular substances. Slides mounting can be done by hand or by an automatic slide mount. The mounting media is represented by the Eukitt gelatine.

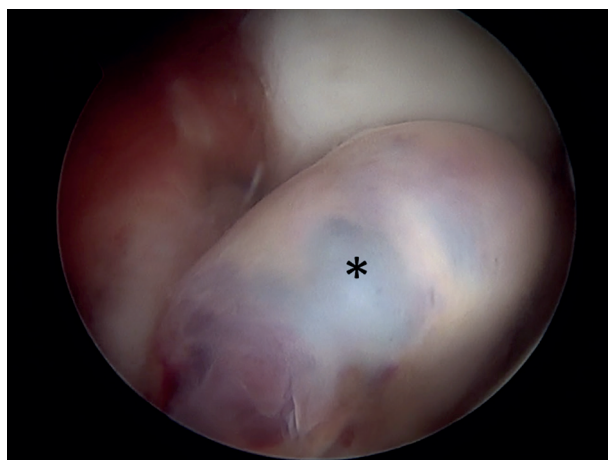
This study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki as revised in 2001 and an informed written consent was obtained from all patients participating in the study.

Results

In thirteen of 126 patients (10,3%) a pedunculated nodule adhering to the anterolateral part of the ACL near tibial insertion was identified during the diagnostic arthroscopy. In objective examination all patients showed joint instability at Lachman and Jerk tests. Only in three patients of the study group (23%) we appreciated the presence of a noise (clunk) in extension and consequent loss of complete extension in the order of 8°-10°. Patients symptoms before surgery are resumed in table 1. The mean interval between trauma and surgical treatment was 2 months (with a range of 1-4 months). At the time of the surgical excision the lesions appeared fixed to the anterolateral part of the native ACL. After lesion removal, the whole range of motion was restored in all patients except for one case where we found an extension deficit of 3-4°. This was completely recuperated with a post-operative period of physical rehabilitation. Three months after

Table 1. Patients' Symptoms before Revision Surgery.

	Age (years)	Progressive loss of extension	Pain at extension	Audible Clunk at extension	Discomfort during walking
M	28	-	+	-	+
F	24	+	+	+	+
M	26	-	+	-	+
M	39	+	+	+	+
M	31	-	+	-	+
M	34	-	+	-	+
M	25	-	+	-	+
M	26	+	+	+	+
F	30	-	+	-	+
M	48	-	+	-	+
M	24	-	+	-	+
M	24	-	+	-	+
M	54	-	+	-	+

**Figure 1.** Arthroscopic view of the cyclops nodule in the intercondylar notch of the femur with a macroscopically histological aspects of a “blue eye”, hence the name Cyclops(*).

removal of the nodule the patients had no pain at terminal extension. During the final follow-up examination, 6 months after the operation, none of the patients reported pain at terminal extension or instability and they were all able to resume their previous activities.

Histologic specimens were available in all 13 patients. The histological studies showed proliferation of dense fibroelastic polypoid nodules (fig. 1), of whitish color, with an average size from 4 x 4 mm to 7 x 13 mm (Table 2).

Microscopic analysis shows proliferation of dense connective tissue, fibroelastic, hyaline, coated with flat epithelial cells similar to synoviocytes (fig. 2).

The histological aspect of the nodule is very similar to the structure of the tendons or fibrous tissue of the ligaments. Vascular proliferation, sometimes glomeruloid, extravasation hemorrhaging, siderophages and evidence of thromboangitis (fig. 3-7).

These macroscopically histological aspects are presented as a bluish focal transparency reminiscent of a “blue eye”, hence the name Cyclops (fig. 1).

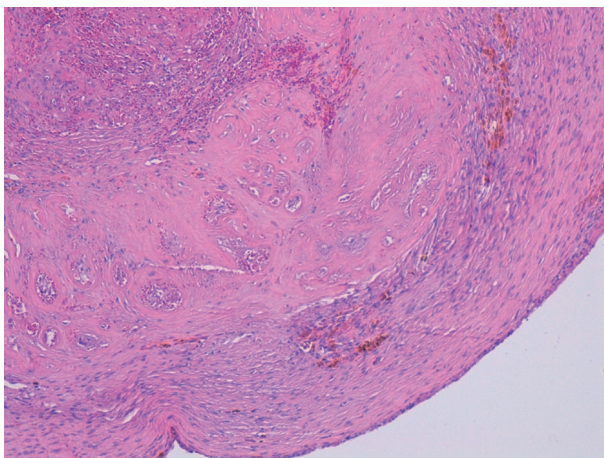
Discussion

In 1990 Jackson and Schaefer (1) described for the first time the cyclops syndrome lesion as a mass of dense fibrous connective tissue rich in newly formed vessels, with the presence of cartilage, newly formed bone tissue and necrotic lamellar bone. In their opinion, the nodule was caused by bone and cartilage residues remaining in the joint after tunnel drilling.

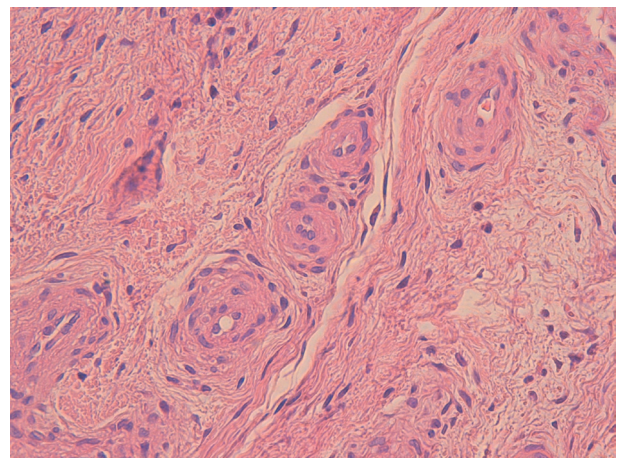
Marzo et al (21) suggested that the irritating stimulus due to the contact between the graft and the intercondylar notch might induce an inflammatory response with the production of granulation tissue. Delcogliano et al (3) found no cartilaginous tissue or

Table 2. Arthroscopic and Histologic Finding (*patients with loss of extension).

Nodule size (mm)	Diffuse fibroproliferation	Sclerosing thromboangitis	Tissue identical to the structure of the ligament
10x10*	+	-	+
7x6	+	+	+
9x10*	+	-	+
6x7	+	+	+
9x6	+	+	+
7x13*	+	+	+
4x4	+	+	+
10x5	+	-	+
7x8	+	+	+
5x8	+	+	+
11x6	+	+	+
6x7	+	-	+
7x7	+	+	+

**Figure 2.** Histologic picture of a cyclops lesion show proliferation of dense connective tissue, fibroelastic, hyaline, coated with flat epithelial cells similar to synoviocytes (4X)

necrotic bone lamellae within the lesion and concluded that microtrauma and micromotion between the bone rim of the tibial tunnel and the graft might be responsible for the formation of granulation tissue and the resulting nodule. In addition three studies have recently discovered some risk factors that we consider significant for the development of the syndrome: Fujii et al (5) have shown in their study that a considerably smaller intercondylar notch is related to increased development of cyclops lesions. Delaloye JR et al (2)

**Figure 3.** Vascular Glomeruloid Proliferation (10X)

conducted a study, in a large cohort of patients, where they showed how the failure to regain full extension in the early postoperative period was the only significant risk factor for cyclops syndrome after ACLR, while Pinto FG et al (22) have shown that persistent hamstring contracture after ACLR is associated with an increased risk of subsequent Cyclops syndrome.

The exact cause of the formation of cyclops lesions resulting from an ACL trauma is still uncertain, so to clarify we have tried to improve two aspects, lacking in previous studies regarding the cyclops: an

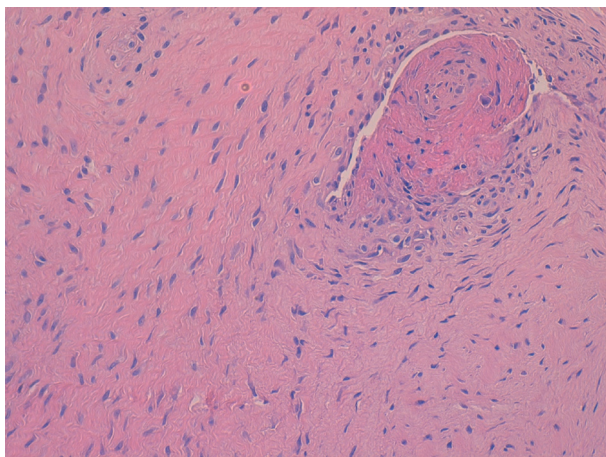


Figure 4. Parietal thrombus and widespread connective tissue proliferation (10X)

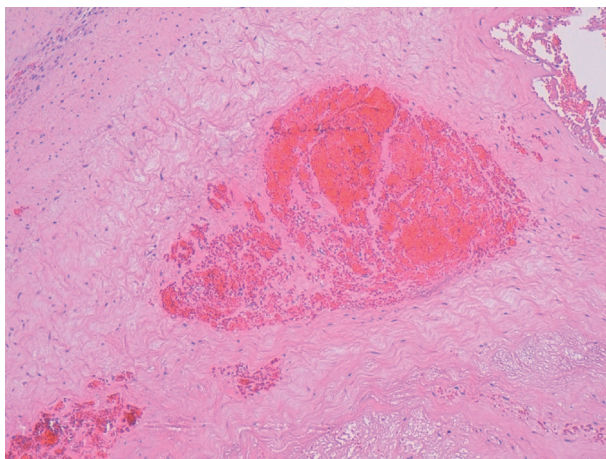


Figure 5. Extravasation hemorrhaging (10X)

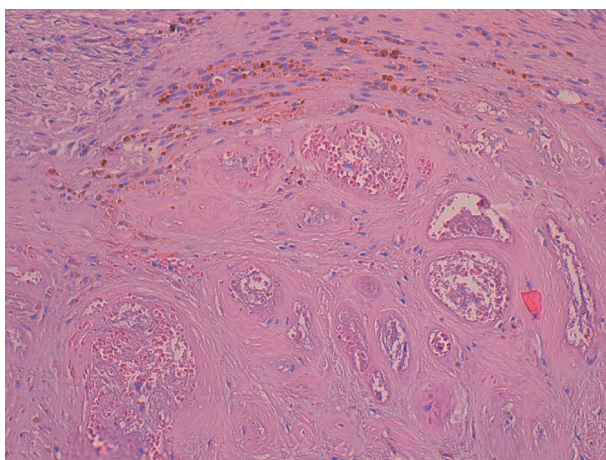


Figure 6. Findings of thromboangiitis with traces of siderophages (10X)

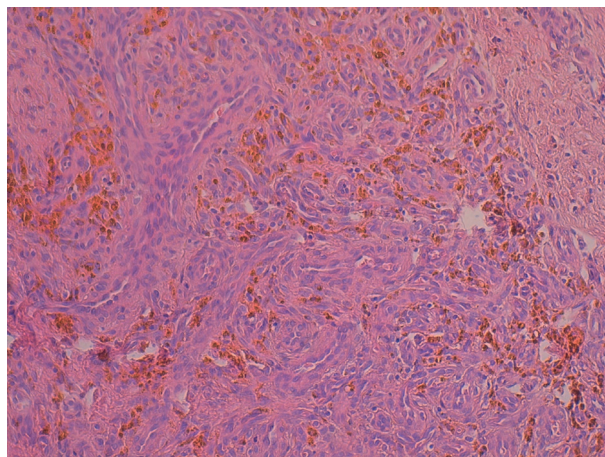


Figure 7. Siderophages (10X)

in-depth histological analysis and better positioning of the arthroscopic portals. In recent years, few papers have shown a new aspect of cyclops syndrome: the presence of cyclops lesions following a rupture of the ACL without surgical reconstruction (11-16). Our experience confirms what has been reported in these studies and specifically the location at the native tibial ligament insertion area, the histological demonstration of the absence of cartilage tissue or lamellar bone tissue and the presence of nodules with numerous newformed vessels in the context of a fibrous tissue: these findings indicate that the cyclops lesions develop like a reactive fibroproliferative process following the rupture of the ACL fibers, as scar reaction to the trauma. However, in our experience, localization and histological analysis indicate that the nodule was formed at the time of ligament damage by the torn fibers. Therefore, we agree with Tonin et al (14) and we can confirm that surgical reconstruction of the ACL is not the only condition in which the Cyclops Sd develops. We have also seen that only nodules of a minimum diameter size of 0.9 cm^2 are symptomatic while smaller lesions have been only an occasional finding during the arthroscopic procedure: we can conclude that in addition to the histological composition of the nodule, a minimal measure is needed to determine the symptoms in affected patients, as we shown in Table 2. In accordance with Muelnner et al (6) we can assert that our asymptomatic lesions correspond to cyclopid lesions.

Last but not least the technique to approach arthroscopy plays a crucial role. As described by Calvisi et Al (18) we have used a modification of Patel midpatellar portal (mMPP) that may offer several advantages when compared with the standard arthroscopic portals. Patel's original mMPP has been shifted more proximally, allowing insertion of the arthroscope that is higher and closer to the midline. This provides a wider coronal view, avoiding the fat pad and instrument crowding and offering a better view to manage the cyclops lesions in our case.

Our study has some limitations such as the small numbers of patients, a condition that prevented a statistical analysis from being performed, and the lack of MRI analysis(17).

Although, due to the relative rarity of this clinical scenario it was difficult to collect a larger patient population.

In conclusion from our evidence and from literature data we can assert that the cyclops syndrome recognizes several etiopathogenetic causes. Cyclops lesions are found both in patients with a re-rupture of the ACL graft, both in patients with a rupture of the native ACL before the reconstruction procedure.

We found that for size < of 0.9 cm² the nodules are usually asymptomatic and according to our experience, the use of surgical technique arthroscopy through mMPP arthroscopic portal has obvious advantages in the detection of these cyclops lesions and in the best post-surgical outcome: in fact, in accordance with literature, it is important to perform an accurate debridement of the articulation during a primary ACL reconstruction in order to avoid post-operative knee loss of extension.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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Correspondence:

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Giuseppe Aloisi, MD

Department of Life Health & Environmental sciences",

University of L'Aquila, Unit of Orthopaedics and

Traumatology, DELTA6 building,

Via Spennati snc, 67100 Coppito (AQ)

Phone number: +39 0862434948

Email: giuseppe.aloisi@graduate.univaq.it

ORCID: 0000-0003-1470-7253